

VESSEL OCCLUDER ADVANCEABLE OVER AN INFUSION CATHETER**PRIORITY CLAIM**

[0001] This application claims priority to U.S. Provisional Application Serial No. 63/616,538 entitled “Vessel Occluder Advanceable Over an Infusion Catheter,” filed on December 30, 2023, and to U.S. Provisional Application Serial No. 63/568,950 entitled “Vessel Occluder Advanceable Over an Infusion Catheter,” filed on March 22, 2024, the entire contents of all of the applications identified above are hereby incorporated by reference herein.

FIELD OF INVENTION

[0002] The system and methods described herein relate generally to intravenously treating a target organ for cancer or other diseases.

BACKGROUND OF INVENTION

[0003] Systemic treatments are often used to treat disease within a patient. The effectiveness of some such systemic treatments can vary due at least in part to the therapy (e.g., a radio-embolization agent, a biologic agent and/or other treatment formulation) not reaching target tissue. For example, in the treatment of diseases such as cancer and/or diabetes, it may be desirable to deliver biological cells to an organ where efficient and safe engraftment can be achieved.

[0004] Systemic chemotherapy is often ineffective at least in part due to an insufficient drug concentration within the tumor because of dose-limited toxicity in bone marrow and epithelial tissue. Another complication can be the resulting occurrence of peripheral neuropathy. Since systemic chemotherapy is limited in its effectiveness or can have significant complications, treatments other than systemic chemotherapy can be desirable for many types of cancer patients.

[0005] One alternative treatment includes local intra-arterial delivery of a therapeutic agent, particularly for the treatment of tumors. Intra-arterial infusion allows higher drug concentration to reach a tumor. Furthermore, intra-arterial chemotherapy can also take advantage of the first pass effect of chemotherapeutics, generating higher-level drug concentrations at the tumor cell membrane and therefore enhancing cellular drug uptake as compared to intravenous systemic infusion. In addition, local delivery of a therapeutic can reduce systemic side effects which otherwise result when a drug disperses.

[0006] Standard end-hole catheters permit limited control of infused local treatment. Contribution of the infusion adds local volume into a nearly incompressible system. The infusion treatment will flow from an area of high pressure to an area of lower pressure. The added fluid volume of the treatment is forced to move somewhere and, if the downstream resistance and pressure is higher than the upstream resistance, reflux to non-target areas will occur.

[0007] Pressure-controlled therapeutic delivery devices in the form of an infusion catheter having an integrated microvalve affixed at the distal end of the catheter may be used to address some of the limitations of standard end-hole catheters. The microvalve dynamically expands and contracts within a blood vessel in relation to the surrounding fluid pressure in the vessel. A treatment can be infused through the catheter. When the treatment agent is infused, the pressure in the vessel downstream (distal) of the treatment at times can be higher than that upstream (proximal) of the treatment, causing the microvalve to open and block reflux of the agent. In addition, the microvalve permits infusion into the target tissue at high pressure, forcing the treatment into the target tissue.

However, there may be treatment scenarios in which it would be desirable to advance a pressure-controlled therapeutic device into smaller vessels. The smaller vessels may not be sized to accommodate targeted delivery of a microvalve mounted a distal end of a catheter.

BRIEF SUMMARY OF THE INVENTION

[0008] A microvalve treatment system includes a microcatheter and a separate microvalve vessel occluder that is longitudinally movable over the catheter. The microcatheter includes a proximal end and a distal end, an exterior surface, and an infusion lumen extending from the proximal end to the distal end. The catheter is adapted to be advanced to a target location in the vasculature of a patient. Then, once the microcatheter is in the intended locations, the microvalve vessel occluder can be advanced over the exterior surface of the microcatheter to a target location in the vasculature in advance of the therapeutic delivery.

[0009] In one example, the microvalve vessel occluder is coupled to the distal end of a low-profile wire and the wire can be operated to advance the microvalve vessel occluder. In another example, the microvalve vessel occluder is coupled to the distal end of an oversheath which can be advanced over the microcatheter. In one example, the microcatheter includes a physical stop on its outer surface to limit advancement of the microvalve vessel occluder over the microcatheter.

Additionally or alternatively, the microcatheter and microvalve vessel occluder include radiopaque markers to facilitate registration of the microvalve vessel occluder relative to one or more locations on the microcatheter. In some examples, once delivered over the microcatheter, the microvalve vessel occluder on microcatheter can operate as a conventional microvalve catheter within the vessel.

[0010] In another aspect of the present application, a method of administering a fluid comprising a therapeutic agent into a blood vessel of an organ is provided. The method comprises the step for advancing a distal tip at a distal end of a catheter into the blood vessel to a target infusion location. The catheter extends from a proximal end to the distal end and comprises an external surface and a lumen extending from the proximal end to the distal end and opens at a distal orifice passing through the distal tip. The method also comprises advancing a microvalve vessel occluder over the external surface of the catheter to a target occlusion location. The microvalve vessel occluder is longitudinally displaceable over the catheter. The method further comprises infusing the fluid comprising the therapeutic agent through the lumen and out of the distal orifice of the catheter and into the blood vessel.

[0011] In a further aspect of the present application, a method of delivering a therapeutic agent to through a vasculature of a patient to a solid tumor in an organ is provided. The vasculature comprises a blood vessel and a plurality of branches from a network of distal blood vessels having a plurality of bifurcation. The method comprises advancing a distal tip at a distal end of an infusion catheter into a target infusion location within one of the distal blood vessels. The infusion catheter extending from a proximal end to the distal end, the infusion catheter comprises a lumen extending from the proximal end to the distal end and opens at a distal orifice passing through the distal tip, wherein the distal blood vessel is in fluid communication with the solid tumor. The method also comprises advancing an occluder distally over the infusion catheter to a target occlusion location in the blood vessel to partially occlude blood flow past the target occlusion location. The occluder is longitudinally displaceable over the infusion catheter. The method further comprises infusing a fluid comprising a therapeutic agent through the lumen and out of the distal orifice of the infusion catheter and into the distal blood vessel. The target infusion location is at least one bifurcation distal of the target occlusion location in the blood vessel.

[0012] In a further aspect of the present application, a treatment system for delivering a therapeutic agent within a vasculature of a patient is provided. The treatment system comprises a

flexible microcatheter comprising a proximal end, a distal portion extending to a distal end, an outer diameter, and a lumen having an inner diameter extending from the proximal end to a distal orifice located at the distal end. The treatment system further comprises a flexible catheter comprising a proximal end, a distal portion extending to a distal end, an inner diameter, a lumen extending from the proximal end to a distal orifice located at the distal end and having an inner diameter, and a microvalve vessel occluder attached to the flexible catheter.

[0013] These and other objects, features, and advantages of the exemplary embodiments of the present disclosure will become apparent upon reading the following detailed description of the exemplary embodiments of the present disclosure, when taken in conjunction with the entire specification.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] Further objects, features and advantages of the present disclosure will become apparent from the following detailed description taken in conjunction with the accompanying Figures showing illustrative examples of the present disclosure.

[0015] Fig. 1 is an assembly side elevation view of a microcatheter microvalve treatment system described herein.

[0016] Fig. 2 is a side elevation of the treatment system of Fig. 1, with the microvalve vessel occluder deployed to a first position along the length of the microcatheter.

[0017] Fig. 3 is a side elevation of the treatment system of Fig. 1, with the microvalve vessel occluder deployed to a second position along the length of the microcatheter.

[0018] Fig. 4 is a side elevation of another example of a treatment system, with the microvalve vessel occluder deployed to a first position along the length of the microcatheter.

[0019] Fig. 5 is an enlarged cross-section along line 7-7 in Fig. 4 of the microcatheter.

[0020] Fig. 6 is an enlarged cross-section along line 7-7 in Fig. 4 of a tubular structure of the microvalve vessel occluder.

[0021] Fig. 7 is an enlarged cross-section along line 7-7 in Fig. 4 through the tubular structure of the microvalve vessel occluder mounted on the microcatheter.

[0022] Fig. 8 is a side elevation of yet another example of a treatment system, with the microvalve vessel occluder deployed to a first position along the length of the microcatheter.

[0023] Figs. 9 through 11 illustrate a method of treatment using the treatment system described

herein.

[0024] Fig. 12 illustrates another method of treatment using the treatment system described herein.

[0025] Fig. 13 illustrates yet another method of treatment using the treatment system described herein.

[0026] Fig. 14 is an assembly side elevation view of another example of microcatheter microvalve treatment system described herein.

[0027] Fig. 15 is a side elevation of the treatment system of Fig. 14, with the microvalve vessel occluder advanced along the length of the microcatheter and the microvalve vessel occluder in a non-deployed configuration.

[0028] Fig. 16 is a side elevation of the treatment system of Fig. 14, with the microvalve vessel occluder advanced along the length of the microcatheter and the microvalve vessel occluder in a partially deployed configuration.

[0029] Fig. 17 is a side elevation of the treatment system of Fig. 14, with the microvalve vessel occluder advanced along the length of the microcatheter and the microvalve vessel occluder in a fully deployed configuration.

[0030] Fig. 18 is an assembly side elevation view of another example of microcatheter microvalve treatment system described herein.

[0031] Fig. 19 is a side elevation of the treatment system of Fig. 18, with the catheter advanced along the length of the microcatheter. and the microvalve vessel occluder in a deployed configuration.

[0032] Fig. 20 is an assembly side elevation view of another example of microcatheter microvalve treatment system described herein.

[0033] Fig. 21A shows an exemplary configuration for a treatment system in an exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient.

[0034] Fig. 21B show an exemplary configuration for a treatment system following the configuration of Fig. 21A in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Fig. 21A.

[0035] Fig. 21C show an exemplary configuration for a treatment system following the configuration of Fig. 21B in the exemplary method of delivering a fluid (*e.g.*, an infusate)

comprising a therapeutic agent of Figs. 21A-21B.

[0036] Fig. 21D show an exemplary configuration for a treatment system following the configuration of Fig. 21C in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Figs. 21A-21C.

[0037] Fig. 22A shows an exemplary configuration for a treatment system in another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient.

[0038] Fig. 22B show an exemplary configuration for a treatment system following the configuration of Fig. 22A in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Fig. 22A.

[0039] Fig. 22C show an exemplary configuration for a treatment system following the configuration of Fig. 22B in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Figs. 22A-22B.

[0040] Fig. 22D show an exemplary configuration for a treatment system following the configuration of Fig. 22C in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Figs. 22A-22C.

[0041] Fig. 23A shows an exemplary configuration for a treatment system in another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient.

[0042] Fig. 23B show an exemplary configuration for a treatment system following the configuration of Fig. 23A in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Fig. 23A.

[0043] Fig. 23C show an exemplary configuration for a treatment system following the configuration of Fig. 23B in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Figs. 23A-23B.

[0044] Fig. 23D show an exemplary configuration for a treatment system following the configuration of Fig. 23C in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Figs. 23A-23C.

[0045] Fig. 24A shows an exemplary configuration for a treatment system in another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient.

[0046] Fig. 24B show an exemplary configuration for a treatment system following the configuration of Fig. 24A in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Fig. 24A.

[0047] Fig. 24C show an exemplary configuration for a treatment system following the configuration of Fig. 24B in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Figs. 24A-24B.

[0048] Fig. 24D show an exemplary configuration for a treatment system following the configuration of Fig. 24C in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Figs. 24A-24C.

[0049] Fig. 25A shows an exemplary configuration for a treatment system in another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient.

[0050] Fig. 25B show an exemplary configuration for a treatment system following the configuration of Fig. 25A in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Fig. 25A.

[0051] Fig. 25C show an exemplary configuration for a treatment system following the configuration of Fig. 25B in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Figs. 25A-25B.

[0052] Fig. 25D show an exemplary configuration for a treatment system following the configuration of Fig. 25C in the exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent of Figs. 25A-25C.

[0053] Fig. 26 is an assembly side elevation view of another example of a treatment system described herein.

[0054] Fig. 27 is an assembly side elevation view of another example of a treatment system described herein.

[0055] Fig. 28A is an assembly side elevation view of another example of a treatment system described herein.

[0056] Fig. 28B shows an enlarged side view of the portion around the first and second occluders of the exemplary treatment system of Fig. 28A marked by a dashed box.

[0057] Fig. 28C shows exemplary occluder patterns for the first and second occluders of the exemplary treatment system of Figs. 28A and 28B.

[0058] Fig. 29 is an assembly side elevation view of another example of a treatment system described herein.

[0059] Fig. 30 is an assembly side elevation view of another example of a treatment system described herein.

[0060] Fig. 31 is an assembly side elevation view of another example of a treatment system described herein.

[0061] Fig. 32 is an assembly side elevation view of another example of a treatment system described herein.

[0062] Fig. 33 is an assembly side elevation view of another example of a treatment system described herein.

[0063] Fig. 34 is an assembly side elevation view of another example of a treatment system described herein.

[0064] Fig. 35 illustrate a method of treatment using the treatment systems described herein.

[0065] Fig. 36 illustrate a method of treatment using the treatment systems described herein.

[0066] Fig. 37 illustrate concentrations of infusate delivery using the treatment system described herein.

[0067] Fig. 38 is a table summarizing the parameters of the study of Example I conducted using an exemplary treatment system described herein.

[0068] Fig. 39 is a graph summarizing the Therapeutic Intensity resulting from the study of Example I described herein.

[0069] Fig. 40 is a graph summarizing the Dose within a Tumor resulting from the study of Example I described herein.

[0070] Throughout the drawings, the same reference numerals and characters, unless otherwise stated, are used to denote like features, elements, components or portions of the illustrated embodiments. Moreover, while the present disclosure will now be describe in detail with references to the figures, it is done so in connection with the illustrative embodiments and is not limited by the particular embodiments illustrated in the figures and the appended paragraphs.

DETAILED DESCRIPTION OF THE INVENTION

[0071] Unless defined otherwise, all technical and scientific terms used herein have the same meaning commonly understood to one of ordinary skill in the art to which this invention pertains. Otherwise, certain terms used herein have the meanings as set in the specification. All patents, published patent applications and publications cited herein are incorporated by reference as if set forth fully herein. It is noted that as used herein and in the appended claims, the singular forms “a,” “an,” and “the” include plural reference unless the context clearly dictates otherwise.

[0072] Throughout this specification and the claims which follow, unless the context requires otherwise, the word “comprise,” and variations such as “comprises” and “comprising,” will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps. When used herein the term “comprising” can be substituted with the term “containing” or “including” or sometimes when used herein with the term “having.”

[0073] As used herein, the conjunctive term “and/or” between multiple recited elements is understood as encompassing both individual and combined options. For instance, where two elements are conjoined by “and/or,” a first option refers to the applicability of the first element without the second. A second option refers to the applicability of the second element without the first. A third option refers to the applicability of the first and second elements together. Any one of these options is understood to fall within the meaning, and therefore satisfy the requirement of the term “and/or” as used herein. Concurrent applicability of more than one of the options is also understood to fall within the meaning, and therefore satisfy the requirement of the term “and/or.”

[0074] The term “subject” or “patient” as used herein refers to an animal, and in one example a mammal. According to particular embodiments, the subject is a mammal including a non-primate (e.g., a camel, donkey, zebra, cow, pig, horse, goat, sheep, cat, dog, rat, rabbit, guinea pig, marmoset or mouse) or a primate (e.g., a monkey, chimpanzee, or human). In particular embodiments, the subject or patient is a human.

[0075] With reference to the following description, the terms “proximal” and “distal” are defined in reference to the hand of a user of the devices and systems described herein, with the term “proximal” being closer to the user’s hand, and the term “distal” being further from the user’s hand such as to often be located further within a body of the patient during use.

[0076] The present application generally relates a method of delivering a fluid (also referred

herein as an infusate) via a vascular system of an organ of a subject to a location within the organ that is in fluid communication with the vascular system. The method may include delivering a fluid to a location within the organ that is near or adjacent to a tumor, in particular, a solid tumor, or abnormal tissue within the organ. The tumor may be a cancerous tumor, a malignant tumor, or a benign tumor. In one example, a method of the present application delivers a therapeutic agent to the tumor within the organ. The tumor is in fluid communication with the vascular system (*e.g.*, blood vessels, such as, arteries or veins) of the organ where blood flowing through the vascular system reaches the tumor. As will be explained further below, the methods described herein provide improved penetration of the infusate or therapeutic agent to the tumor. The methods and systems of the present application is described herein with respect to delivering a fluid and/or a therapeutic agent to a tumor within an organ. However, it is contemplated that such methods and systems are also applicable to delivery of a fluid and/or a therapeutic agent to abnormal tissue within an organ (*e.g.*, uterine fibroids).

[0077] In one example, a method for delivering a therapeutic agent to a tumor in an organ (*e.g.*, liver) of a patient is described herein. The tumor is in fluid communication with a vascular system of the organ. The method comprises advancing an occluder through the vascular system in the organ (*e.g.*, liver) and positioning the occluder within the vascular system at a location proximal of the tumor. The vascular system comprises a blood vessel (*e.g.*, an artery or a vein, and branches thereof). The vascular system may comprise a blood vessel and branches from a plurality of bifurcations distal (*i.e.*, downstream for arteries and upstream for veins) of the blood vessel. In one example, the vascular system may be an artery and branches from a network of arterial blood vessels having a plurality of bifurcations downstream (*i.e.*, further distal of the artery). In another example, the vascular system may be a vein and branches from a network of venous blood vessels having a plurality of bifurcations upstream (*i.e.*, further distal of the vein). The occluder when positioned at a desired location (*i.e.*, a target occlusion location) within a target occlusion blood vessel of the vascular system wholly, partially or intermittently blocks fluid flow in the target occlusion blood vessel in a distal to proximal direction. In other words, the occluder acts as a complete, partial or intermittent barrier to flow about the occluder and through the target occlusion blood vessel in a distal to proximal direction.

[0078] Although the above description identifies the liver as an example of an organ in which the methods of the present application may be used, it is contemplated that the methods describe

herein may be useful for delivering a therapeutic agent to the liver, pancreas, kidney, spleen, prostate, uterus, small intestine and other organs in need of targeted delivery of the therapeutic agent to a tumor within the organ. For example, the organ may be the liver and the target occlusion location is in a right hepatic artery, a left hepatic artery, a common hepatic artery, or any branches thereof. In one example, the organ may be the pancreas and the target occlusion location is in a gastroduodenal artery, a splenic artery, or any branches thereof feeding the pancreas. In another example, the organ may be the kidney and the target occlusion location is in a renal artery, or any branches thereof. In a further example, the organ may be a spleen and the target occlusion location is in a splenic artery. In another example, the organ may be a prostate and the target occlusion location is in a prostatic artery. In a further example, the organ may be a uterus, and the target occlusion location is a uterine artery, or any branches thereof. In a further example, the organ may be the small intestine, and the target occlusion location is a gastroduodenal artery, a superior mesenteric artery, or any branches thereof feeding the small intestine.

[0079] The method also comprises advancing a catheter for delivering an infusate through an infusion lumen of the catheter and through a distal orifice at the distal tip of the catheter in fluid communication with the infusion lumen. The distal orifice of the catheter is advanced to a desired location (*i.e.*, a target infusion location) distal of the occluder for delivering the infusate. The distal orifice is positioned at a target infusion location proximal of the tumor. In particular, the distal orifice is positioned at a target infusion location proximal to, and more specifically, near or adjacent to the tumor that is to be treated with the therapeutic agent. For example, the target infusion location is positioned in fluid communications with a blood vessel immediately distal of the target infusion location (*i.e.*, a downstream artery or an upstream vein) that feeds a first volume of tissue less than a second volume of tissue that is fed by a blood vessel immediately distal of the target occlusion location (*i.e.*, a downstream artery or an upstream vein of the target occlusion location). In one example, the target occlusion location is positioned in a blood vessel (*e.g.*, artery) supplying half of the liver with blood flow, and the target infusion location is placed within a blood vessel within a distal vascular network (*e.g.*, downstream arterial network) of the target occlusion location and supplying less than about half (*e.g.*, about a quarter) of the liver or other organ (as identified above) with blood flow. In one example, the target occlusion location is positioned in a blood vessel (*e.g.*, vein) draining half of the liver's blood flow, and the target infusion location is placed within a blood vessel within a distal vascular network (*e.g.*, upstream venous network) of

the target occlusion location and draining less than about half (*e.g.*, about a quarter) of the blood flow of the liver or other organ (as identified above). In some examples, the target infusion location is position in fluid communications with a distal blood vessel (*e.g.*, downstream arterial vessel) that feeds a first volume of tissue at least 10% less, at least 20% less, at least 30% less, at least 40% less, at least 50% less, at least 60% less, at least less 70% less, at least 80% less, at least 90% less, from at or about 10% to at or about 90% less, or from at or about 30% to at or about 80% less than a second volume of tissue that is fed by a downstream blood vessel in fluid communications with the target occlusion location.

[0080] In another example, the target infusion location is positioned at least one bifurcation of branches distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion blood vessel. In particular, the target infusion location is positioned a plurality (*i.e.*, two or more) bifurcations of branches distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion blood vessel. In some examples, the target infusion location is positioned two, three, four, five, or six bifurcations of branches distal (*i.e.*, distal) of the target occlusion blood vessel. In a particular example, the target infusion location is positioned two or three bifurcations of branches distal (*i.e.*, distal) of the target occlusion blood vessel.

[0081] In a further example, the organ is the liver and the target infusion location is positioned about 20 cm or less from the target occlusion location. In particular, the organ is the liver and the target infusion location is positioned about 15 cm or less from the target occlusion location. More particularly, the organ is the liver and the target infusion location is positioned about 10 cm or less from the target occlusion location.

[0082] After the distal orifice of the catheter is positioned at the target infusion location, the infusate is delivered out of the distal orifice and into a target infusion blood vessel distal of the distal orifice. In some examples, the infusate may be delivered via the treatment system at a flow rate that causes increase in pressure distal of the target occlusion location as compared to without the infusion. The increased pressure forces the fluid and/or therapeutic agent deeper into the tumor. In some examples, the infusate may be delivered at a flow rate that causes increase in pressure distal of the target occlusion location as compared to without the infusion by at or about 10%, at or about 50%, at or about 100%, at or about 110%, at or about 150%, at or about 200%, at or about 300%, at or about 400%, or at or about 500%. In some examples, the infusate may be delivered at a pressure higher by from at or about 10% to at or about 500%, from at or about 50%

to at or about 500%, from at or about 100% to at or about 500%, from at or about 110% to at or about 500%, from at or about 150% to at or about 500%, from at or about 200% to at or about 500%, from at or about 300% to at or about 500%, from at or about 400% to at or about 500%, from at or about 10% to at or about 50%, from at or about 10% to at or about 100%, from at or about 10% to at or about 110%, from at or about 10% to at or about 150%, from at or about 10% to at or about 200%, from at or about 10% to at or about 300% than a pressure distal of the target occlusion location without the infusion by an amount. In some examples, the infusate may be delivered at a flow rate that causes increase in pressure distal of the target occlusion location to a blood pressure from at or about 80 mmHg to at or about 400 mmHg, from at or about 80 mmHg to at or about 200 mmHg, or from at or about 80 mmHg to at or about 300 mmHg. In some examples, the infusate may be delivered at a flow rate of from at or about 0.2 mL/s to at or about 10 mL/s, from at or about 0.5 mL/s to at or about 5 mL/s, or from at or about 1 mL/s to at or about 3 mL/s.

[0083] In some examples, the infusate may be delivered in one or more deliveries may for example, comprise one delivery, two deliveries, three deliveries, five deliveries, ten deliveries, more than ten deliveries, between one delivery and ten deliveries. One or more delivery durations may, for example, comprise one or more deliveries for a length of 0.5 seconds, 5 seconds, 10 seconds, 0.5-10 seconds, and/or more than 10 seconds. One or more durations between a plurality of deliveries may, for example, comprise one or more durations for a length of 1 second, 3 seconds, 30 seconds, 60 seconds, 120 seconds, more than 120 seconds, less than 1 second, 1-3 seconds, 1-30 seconds, 1-60 seconds, and/or 1-120 seconds.

[0084] The methods described herein may be implemented using a treatment system for delivering a fluid through a vascular system of an organ of a patient. In one example, the treatment system may be useful for delivering a therapeutic agent to a tumor within an organ of the patient. An exemplary treatment system for delivering a therapeutic agent via a vascular system of an organ of a patient may, for example, comprise one or more tubular elements, and an occluder. The treatment system may also comprise one or more sensing wires, each comprising one or more sensing elements, as discussed further below. The distal end of the sensing wire and/or a sensing element may be adjusted to any suitable sensing location for measuring a characteristic, such as, for example, fluid pressure, vascular pressure, infusion pressure, flow rate, and/or infusion volume within the blood vessel. For example, the distal end of the sensing wire and/or a sensing element

may be located on a distal portion of a tubular element, on a proximal portion of a tubular element, on an outer surface of an occluder, or within an interior of an occluder. The treatment system may further comprise, one or more hubs, one or more guidewires, one or more pushers, one or more cables, and/or one or more handles. Each of these additional elements are discussed in further detail below. Additionally, the distal end of the sensing wire and/or a sensing element may be adjusted to be within a hub, on a guidewire, or within a handle. The treatment system may, for example, be used in a method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent to a tumor in fluid communication with a vascular system of an organ of a patient.

[0085] The infusate delivered via the treatment systems described herein may comprise contrast media, saline solution, dextrose solution, a fluid pharmaceutical formulation comprising one or more therapeutic agents, or other biologically compatible solution for infusing into blood vessels of an organ of a human. The one or more therapeutic agents may, for example, comprise an embolizing agent, a radioembolization agent, a biologic agent, a chemotherapeutic agent, a drug, a contrast agent, and/or other treatment agent. The therapeutic agent(s) may be present in the pharmaceutical formulations as an agent in solution, an agent in suspension, a foam agent, a gel agent, a bead agent, an agent coated bead, a microsphere agent, and/or an agent coated microsphere. In some examples, the dextrose solution may be a 5% dextrose solution. In some examples, the contrast media may comprise a contrast agent and/or a contrast solution.

[0086] The tubular element is an elongated structure having a proximal end and a distal end. In one example, the cross-sectional shape of the tubular element is circular. However, the tubular member may have any suitable cross-sectional shape. The tubular element also comprises an inner lumen extending therethrough from the proximal end to the distal end, and an outer surface parallel to the inner lumen. The tubular element may be, for example, a catheter or a tubular member. An example of a suitable catheter is a microcatheter. In some examples, the microcatheter may be a flexible microcatheter. The microcatheter may have a tapered distal end and/or may have a wider proximal portion that tapers to a narrower distal portion. In some examples, the tubular element may comprise a tubular structure, such as, for example, a short tubular structure (as defined further below), a metal or polymer collar, a portion/segment of a catheter, a hypotube, and/or a portion of a hypotube and/or an oversheath.

[0087] The occluder may be any suitable structure, when inserted into a blood vessel that wholly, partially or intermittently blocks fluid flow in the blood vessel in a distal to proximal

direction. The occluder may, for example, comprise a microvalve vessel occluder (*e.g.*, a filter valve), a dynamic vessel occluder, a full vessel occluder, a partial vessel occluder, a balloon occluder, and/or a compliant membrane containing an occluder fill material. In one example, the occluder is a dynamic occluder that dynamically adjusts its configuration in response to fluid pressures within a blood vessel to intermittently occlude the blood vessel. The dynamic occluder may be movable across an expanded configuration (*e.g.*, a partially expanded configuration or a fully expanded configuration) or a collapsed configuration (*e.g.*, a fully collapsed configuration or a partially collapsed configuration).

[0088] In one example, the occluder, when inserted into a blood vessel partially blocks fluid flow in the blood vessel in a distal to proximal direction. The occluder may partially block fluid flow in the blood vessel such that distal (*i.e.*, downstream in arteries) vascular pressure is reduced. The magnitude of reduction of the distal vascular pressure is sufficient to elicit vascular adaptive response and/or reduction in normal tissue volume and therefore, alters proportion of blood flow to normal tissue and to the tumor. The reduction in distal vascular pressure is believed to induce a higher proportion of blood flow to the tumor as compared to normal tissue. It is believed that as a fluid and/or therapeutic agent is infused into the blood vessel, the reduction in distal vascular pressure increases the proportion of the fluid and/or therapeutic agent flowing to the tumor because of blood flow pattern changes induced by the reduction in distal vascular pressure.

[0089] In a further aspect of the present application, a method of delivering a therapeutic agent in a target vessel of a patient is provided. The method comprises advancing a treatment system (*e.g.*, a partial vessel occluder system) into a target vessel of a patient. The method also comprises expanding an occluder proximal of the distal orifice to occlude (*e.g.*, partially occlude) the target vessel to reduce distal blood pressure and/or flow at the target occlusion location. The occluder (*e.g.*, partial vessel occluder) reduces pressure sufficiently to elicit an adaptive response in distal (*i.e.*, downstream in arteries and upstream in veins) tissues. The adaptive response results in a higher proportion of blood flow to abnormal or cancerous tissue. The method further comprises advancing a second component of the system, comprising a catheter having infusion lumen extending from a proximal end to a distal end and opening to a distal orifice into the distal vascular network past the partial vessel occluder to a target infusion location. The target occlusion location and the target infusion location relate to each other as discussed above. The distal vascular network supplying (for an artery) or withdrawing blood flow from (for a vein) a least a portion of abnormal

or cancerous tissue. The method involves infusing a therapeutic agent through the second component into the vessel supplying (for an artery) or draining blood flow from (for a vein) the abnormal or cancerous tissue, the blood proportion to the abnormal or cancerous tissue being substantially increased due to the adaptive vascular response caused by the proximal vascular occluder.

[0090] In some examples, the occluder may partially block fluid flow in the blood vessel such that distal (*i.e.*, downstream in arteries) vascular pressure is reduced by about 10% to about 80%, about 10% to about 70%, about 10% to about 60%, about 10% to about 50%, about 10% to about 40%, about 20% to about 80%, about 20% to about 70%, about 20% to about 60%, about 20% to about 50%, about 20% to about 40%, about 30% to about 80%, about 30% to about 70%, about 30% to about 60%, about 30% to about 50%, or about 30% to about 40% as compared to a normal vascular pressure (*i.e.*, distal vascular pressure when the blood vessel is not partially blocked by the occluder). Preferably, the occluder partially blocks fluid flow in the blood flow such that distal vascular pressure is reduced by 10% to 80%, more preferably, by 20% to 60% and more preferably by 20% to 40% as compared to a normal vascular pressure. In an example, the occluder partially blocks fluid flow in the blood flow such that distal vascular pressure is reduced by 20% to 70%, or more preferably, by 30% or 60%.

[0091] In a particular example, the microvalve vessel occluder is a dynamic filter valve that dynamically adjusts its configuration in response to fluid pressures within a blood vessel to intermittently occlude the blood vessel. More particularly, the dynamic filter valve may expand to an expanded configuration that partially or completely occludes the blood vessel when the fluid pressure is higher on the distal side than the proximal side of the dynamic filter valve. The dynamic filter valve may contract to a collapsed configuration to allow fluid flow past the dynamic filter valve when the fluid pressure is higher on the proximal side than the distal side of the dynamic filter valve. The collapsed configuration has a smaller diameter than the expanded configuration.

[0092] The microvalve vessel occluder may include a filamentary structure comprising a plurality of filamentary strands, such as, for example, a braided filamentary structure, a tubular braid structure or a tubular parallel filamentary structure, each of which are described in further detail below. The microvalve vessel occluder may further comprise a filter or membrane covering at least a portion of (*i.e.*, a portion of or completely covering) the filamentary structure. The filter or membrane may be fluid permeable or fluid impermeable. In some examples, a fluid permeable

filter membrane may be a porous polymeric filter. Certain examples of different combinations of a filamentary structure and a filter/membrane within a microvalve vessel occluder may include a braided filamentary structure and a porous polymeric filter; a braided filamentary structure and a fluid impermeable polymeric membrane; a tubular braid structure and a porous polymeric filter; a tubular braid structure and a fluid impermeable polymeric membrane; a filamentary structure and a fluid impermeable polymeric membrane; and/or a filamentary structure and a porous polymeric filter.

[0093] In one example, the occluder is attached to an external surface of a tubular member. The occluder may be attached to the external surface of the tubular member at a proximal portion of the tubular member, at a distal portion of the tubular member, or at an area between a proximal end and a distal end of the tubular member.

[0094] Referring to Figs. 1 and 2, an example of a treatment system 10 herein includes a flexible microcatheter 12 having a proximal end 14 and a distal end 16. An infusion lumen extends from the proximal end 14 to the distal end 16 of the microcatheter and exits through a distal tip 22 at a distal orifice 24. In one example, the microcatheter 12 has a length between two and eight feet long, and an outer diameter of between 0.67 mm and 3 mm (corresponding to catheter sizes 2 French to 9 French).

[0095] In one example, the microcatheter 12 comprises an inner liner, an inner braid, and an outer coating. By way of example, the liner may be comprised of fluorinated polymer such as polytetrafluoroethylene (PTFE), fluorinated ethylene propylene (FEP), polypropylene, and/or polyethylene. By way of example, the liner may be chemically resistant. By way of example, the braid is comprised of metal such as stainless steel, nickel titanium alloy, tungsten, platinum, platinum iridium alloy, a polymer, polyethylene terephthalate (PET), and/or a liquid crystal polymer. By way of example, the braid may comprise reinforcing material. By way of example the braid may comprise a coil of wire. By way of example, the outer coating may be comprised of a thermoplastic elastomer, a polyether block amide thermoplastic elastomeric resin such as Pebax®, polyurethane, polyamide, copolymers of polyamide, polyester, copolymers of polyester, fluorinated polymers, such as PTFE, FEP, polyimides, polycarbonate, aromatic polyether and polyester such as Pellethane®, aliphatic polyether such as Tecoflex®, thermoplastic vulcanizates, ethylene propylene diene monomer rubber such as Santoprene®, silicone rubber another suitable material, any other standard material used in making catheters used in the bloodstream, and/or any

other specialty material used in making catheters used in the bloodstream. By way of example, the microcatheter 12 comprises a hydrophilic coating on the outer coating, the hydrophilic coating may reduce friction and/or improve the trackability of the microcatheter 12. By way of example, the outer coating may comprise multiple segments of different materials along a length of the microcatheter 12. By way of example, the outer coating may comprise one or more softer materials distal to a stiffer material, one or more stiffer materials proximal to a softer material, and/or a stiffer material at the proximal end and a softer material at the distal end of the microcatheter 12.

[0096] A distal portion of the microcatheter is provided with one or more marker bands. In one example, a first marker band 26 is provided adjacent the distal tip 22; additional marker bands 28 may be provided elsewhere along the distal portion of the microcatheter to aid in use of the system; for example, every 10 mm for a length of 60 mm from the distal tip of the catheter 12. By way of example, the one or more marker bands may be comprised of gold, tungsten, platinum, platinum iridium alloy, a radiopaque material, any other standard material used in making catheters used in the bloodstream, and/or any other specialty material used in making catheters used in the bloodstream.

[0097] In one exemplary aspect of the system, a microvalve vessel occluder 30 is provided for displacement relative to, and advancement over, the microcatheter. In one example, the microvalve vessel occluder 30 is formed on a short tubular structure 32. The tubular structure may be, by way of example, 5 - 10 mm in length. The term 'short' is determined with reference to the length of the microcatheter. In one example, the tubular structure is less than 10% the length of the microcatheter. In one example, the tubular structure is less than 5% the length of the microcatheter. In one example, the tubular structure is less than 2% the length of the microcatheter. In certain examples, the tubular structure is less than 5% the length of the microcatheter, less than 2% the length of the microcatheter, and/or less than 1% the length of the microcatheter. The tubular structure 32, by way of example only, may be a metal or polymer collar, portion of a hypotube, or a catheter portion. The microvalve vessel occluder 30 is constructed from a tubular braid of multiple strands in tubular form and coated with a fluid impermeable polymeric membrane or a porous polymeric filter construct. For example, the microvalve vessel occluder 30 may be constructed as described in U.S. Pat. Nos. 8,696,698, 9,968,740, 10,588,636 and/or US Serial No. 17/969,506, filed October 19, 2022, all of which are incorporated by reference herein.

[0098] In general, the tubular braid of the microvalve vessel occluder 30 is comprised of

multiple metal (e.g., stainless steel or nickel-titanium alloy) or polymer filaments or strands in a tubular braided construction, which form a substantially closed shape when deployed and not subject to outside forces. Where polymeric filaments are utilized, the filaments may be composed of PET, polyethylene-naphthalate (PEN), liquid crystal polymer, fluorinated polymers, nylon, polyamide or any other suitable polymer. If desired, when polymeric filaments are utilized, one or more metal filaments may be utilized in conjunction with the polymeric filaments. According to one aspect of the invention, where a metal filament is utilized, it may be of radio-opaque material to facilitate tracking the microvalve vessel occluder its configuration within the body. The filaments are not bonded to each between their ends so to enable them to move relative to each other between their ends. The filaments are spring biased (i.e., they have “shape memory”) to assume a desired crossing angle relative to each other. Between each two adjacent sets of crossing filaments, diamond-shaped interstices, or pixels are formed, with the crossing of the filaments defining vertices of the pixels. The specific shape and size of the pixels is determined by the braid angle between crossing filaments in the tubular braid.

[0099] In some examples, the diameter of the filaments of the microvalve vessel occluder 30 are chosen in the range of 0.025 mm to 0.127 mm, although other diameters may be utilized. In one example, the pitch angle (i.e., the crossing angle assumed by the braided filaments in the fully open deployed position) is chosen in the range of 100° to 150°, although other pitch angles may be used.

[00100] More particularly, the tubular braid of the microvalve vessel occluder 30 operates to expand and contract radially as it is subject to longitudinal displacement between its ends. The radial force the braid exerts is related to the bending strength of the filaments making up the braided structure and the crossing angle at which the braid filaments intersect at the vertices. The closer a filament is to a vertical orientation within the braided structure, the more radial force it will exert. As the tubular braid is displaced laterally (expanded to compressed), the vertices of the pixels of the pixels can move, but the length of the sides (X) of each pixel is fixed.

[00101] The radial forces of expansion of the tubular braid is described by Jedwab and Clerc (*Journal of Applied Biomaterials*, Vol. 4, 77-85, 1993) and later updated by DeBeule (DeBeule et al., *Computer Methods in Biomechanics and Biomedical Engineering*, 2005) as:

[00102]

$$F = 2n \left[\frac{GI_p}{K_3} \left(\frac{2 \sin \beta}{K_3} - K_1 \right) - \frac{EI \tan \beta}{K_3} \left(\frac{2 \cos \beta}{K_3} - K_2 \right) \right]$$

[00103] where K_1 , K_2 , K_3 are constants given by:

$$K_1 = \frac{\sin 2\beta_0}{D_0} \quad K_2 = \frac{2\cos^2 \beta_0}{D_0} \quad K_3 = \frac{D_0}{\cos \beta_0}$$

[00104]

[00105] and I and I_p are the surface and polar moments of inertia of the braid filaments, E is the Young's modulus of elasticity of the filament, and G is the shear modulus of the filament. These material properties along with the initial braid angle (β_0), final braid angle (β), tubular braid diameter (D_0), and number of filaments or strands (n) impact the radial force of the braided valve.

[00106] As will be appreciated by those skilled in the art, the braid geometry and material properties of the filaments are intimately related to the radial force and time constant of the filter valve. Since the filter valve is useful in a variety of vessels of different diameters and flow conditions, each implementation can have a unique optimization.

[00107] In one example, the tubular braid uses twenty-four (24) strands: twelve (12) nickel titanium strands having a diameter of approximately 0.02 mm (0.0008 inch) and twelve (12) nickel titanium strands having a diameter of approximately 0.032 mm (0.00125 inch). This produces a tubular braid having approximately 34 to 38 pixels per linear inch and a braid angle between 120° and 130° when the diameter of the tubular braid is set at 4.5 mm.

[00108] In another example, the tubular braid uses twenty-four (24) strands: twelve (12) nickel titanium strands having a diameter of approximately 0.025 mm (0.001 inch) and twelve (12) nickel titanium strands having a diameter of approximately 0.038 mm (0.0015 inch). This produces a tubular braid having approximately 27 to 31 pixels per linear inch and a braid angle between 120° and 130° when the diameter of the tubular braid is set at 6 mm.

[00109] The tubular braid is coated with fluid permeable polymer filter material or fluid impermeable polymer membrane which covers the filaments and extends across the pixels, such as, for example, the polymer coatings described in U.S. Pat. Nos. 8,696,698, 9,968,740, 10,588,636 and/or US Serial No. 17/969,506. By way of example only, the polymer coating can be coated onto the braid by spraying, spinning, electrospinning, bonding with an adhesive, thermally fusing, mechanically capturing the braid, melt bonding, dip-coating, or any other desired method, to form the coating. The coating should not bind movement of the strands relative to each other.

[00110] In one example, the microvalve vessel occluder 30 is formed by attaching a first end of the coated tubular braid to the tubular construct 32, then everting the tubular braid, and then attaching a second end of the tubular braid at a longitudinally displaced location on the tubular

construct. The microvalve vessel occluder 30 is adapted to be self-expanding and dynamically move based on the relative fluid pressure conditions at opposing proximal and distal sides of the microvalve vessel occluder in a vessel.

[00111] In one example, one or more radiopaque marker bands 34 are provided on the tubular construct 32 at proximal and/or distal portions of the microvalve vessel occluder 30. During use of the device, the *in vivo* positions of the one or more marker bands 34 viewed fluoroscopically or via other imaging technique indicates the location of the microvalve vessel occluder 30 relative to the marker bands 26, 28 on the microcatheter 12 and relative to anatomical landmarks which may be highlighted via imaging with contrast agent.

[00112] The microvalve vessel occluder 30 is sized to be longitudinally displaced over the microcatheter 12, from the proximal end 14 of the microcatheter to the distal end 16 of the microcatheter. In one example, the microcatheter 12 and microvalve vessel occluder 30 are adapted, such that the microvalve vessel occluder is advanceable to a defined position at the distal end of the microcatheter. In particular, the microcatheter has a suitable length for the microvalve vessel occluder 30 to be longitudinally displaced relative to the microcatheter such that when the treatment system 10 is inserted into a target vessel and in place for infusion, the distal end of the microcatheter is positioned at a target infusion location that is in fluid communications with a distal (*i.e.*, downstream in arteries) blood vessel that feeds a first volume of tissue less than (*e.g.*, at least 10% less, at least 20% less, at least 30% less, at least 40% less, at least 50% less, at least 60% less, at least 70% less, at least 80% less, at least 90% less, from at or about 10% to at or about 90% less, or from at or about 30% to at or about 80% less) a second volume of tissue that is fed by a distal blood vessel in fluid communications with a position of the microvalve vessel occluder 30 (*e.g.*, target occlusion location). In one example, the microcatheter has a suitable length for the microvalve vessel occluder 30 to be longitudinally displaced relative to the microcatheter such that when the treatment system 10 is inserted into a target vessel and in place for infusion, the distal end of the microcatheter is positioned at a target infusion location that is in fluid communications with a distal (*i.e.*, upstream in veins) blood vessel that withdraws blood flow from a first volume of tissue less than (*e.g.*, at least 10% less, at least 20% less, at least 30% less, at least 40% less, at least 50% less, at least 60% less, at least 70% less, at least 80% less, at least 90% less, from at or about 10% to at or about 90% less, or from at or about 30% to at or about 80% less) a second volume of tissue, from which a distal blood vessel withdraws blood flow, in fluid communications

with a position of the microvalve vessel occluder 30 (*e.g.*, target occlusion location).

[00113] In some examples, the microvalve vessel occluder 30 can be longitudinally displaced relative to the microcatheter such that when the treatment system 10 is inserted into a target vessel and in place for infusion, the microvalve vessel occluder 30 is positioned at a target occlusion location at least one bifurcation or at least two or more bifurcations (*e.g.*, two, three, four, five, or six bifurcations, more particularly, two or three) of branches upstream (*i.e.*, proximal) of the distal end of the microcatheter. In one example, the microvalve vessel occluder 30 can be longitudinally displaced relative to the microcatheter such that the microvalve vessel occluder 30 is proximal of the of the distal end of the microcatheter by a length of about 20 cm or less, by about 15 cm or less, by about 10 cm or less. In particular, the microvalve vessel occluder 30 can be longitudinally displaced relative to the microcatheter such that the microvalve vessel occluder 30 is proximal of the of the distal end of the microcatheter by a length from at or about 1 cm to at or about 20 cm, from at or about 1 cm to at or about 15 cm or less, or from at or about 1 cm to at or about 10 cm.

[00114] The microcatheter 12 may include a structural stop 40 to define a distal limit to which the microvalve vessel occluder 30 may be advanced over the microcatheter and to prevent the microvalve vessel occluder from being advanced off the distal tip 22 microcatheter. The distal marker 26 may be the structural stop 40. For example, the distal marker 26 may have a diameter or some portion extending radially outwards larger than the inner diameter of the tubular structure 32 of the microvalve vessel occluder 30 to prevent the microvalve vessel occluder from being advanced beyond the distal marker.

[00115] In one example, the microvalve vessel occluder 30 may be positioned over the proximal end 14 of the microcatheter 12 and coupled to a pusher 42, such as a wire, guidewire, cable, or other flexible shaft (all of which shall be referred to as a ‘wire’ herein). The wire 42 can be permanently coupled to the microvalve vessel occluder or removably coupled, such as inserting a Z-bend or a loop 46 at the end of the wire 42 through an eyelet 48 on the tubular structure 32 of the microvalve vessel occluder 30. The wire 42 is sufficiently longitudinally stiff to be advanced through a vessel alongside the microcatheter 12 and push the microvalve vessel occluder 30 over the outside of the microcatheter. The wire 42 controllably advances the microvalve vessel occluder 30 until the microvalve vessel occluder is positioned at the distal end 16 of the microcatheter, *e.g.*, at the distal marker 26. This can be determined under radiographic imaging by reference to the markers 26, 34. Alternatively, by controlled manipulation of the wire 42, the microvalve vessel

occluder 30 can be advanced to an intermediate location along the length of the microcatheter proximal of the distal end of the microcatheter, to arrange markers 34 on the microvalve vessel occluder relative to one of the other markers 28 (as shown in Fig. 3) or arranged over the microcatheter and relative to an anatomical landmark.

[00116] Turning to Fig. 4 through 7, in another example of a treatment system 110, the microcatheter 112 is provided with one or more longitudinal rails 150 formed on an external surface of the microcatheter. The microvalve tubular member 132 includes an inner surface with a mating structure, such as in the form of pairs of brackets 152 adapted to be guided over the rails 150. The rails 150, bracket pairs 152 or other suitable mating structure can be provided interchangeably to the microcatheter 112 and the microvalve tubular member 132. In one example, a stop element 140, as described above, is provided at the distal end of the rails 150. The stop element 140 may be formed on the rails, may be in the form of a radiopaque marker, or may be an independent structure. A wire 142 may similarly be coupled to the tubular member 132 of the microvalve vessel occluder 130 and longitudinally displaced to advance the microvalve vessel occluder 130 over the outside of the microcatheter 112 to the distal end or an intermediate position along the length of the microcatheter. The microvalve vessel occluder 130 may be longitudinally displaced relative to the microcatheter 112 in by the same distances as discussed above with respect to displacement of microvalve vessel occluder 30 over a microcatheter.

[00117] Referring to Figs. 14 through 17, in another example of a treatment system 510, a microcatheter 512 is provided, as described above, in association with a microvalve vessel occluder 530 at the distal end of a pusher 542. The distal end of the pusher 542 is coupled to a proximal end 536 of the microvalve vessel occluder 530. In distinction from the prior examples, the microvalve vessel occluder 530 is originally provided in a tubular non-deployed state. The microvalve vessel occluder 530 is adapted to be advanced over the exterior of the microcatheter 512 in the tubular non-deployed state until a distal end 538 of the microvalve vessel occluder 530 abuts the stop 540 on the microcatheter (Fig. 15). Then, as the pusher 542 is further longitudinally advanced along the microcatheter 512, the pusher asserts a compressive force between the proximal end 536 of microvalve vessel occluder 530 and the stop 540, forcing the distal and proximal ends 536, 538 of the microvalve vessel occluder 530 closer together and moving the microvalve vessel occluder 530 into a partially deployed state in which the diameter of the occluder begins to expand (Fig. 16). Additional longitudinal advancement of the pusher results in the

proximal end 536 of the microvalve vessel occluder moving toward the distal end 538 of the microvalve vessel occluder, in one example of the occluder, the inversion of the distal end 538 of the microvalve vessel occluder, and complete deployment of the microvalve vessel occluder 530. (Fig. 17). The microvalve vessel occluder 530 can be removed by retracting the pusher 542 to cause collapse of the microvalve vessel occluder 530. The stop 540 may include a catch (not shown) to hold the distal end 538 of the microvalve vessel occluder 530 to more easily permit retraction of the proximal end of the microvalve vessel occluder relative to its distal end; the microcatheter and collapsed microvalve vessel occluder are sized to permit removal from the patient together in this form. Further, the microvalve vessel occluder can be withdrawn from the patient in the expanded configuration on the microcatheter without detriment to the patient.

[00118] Turning now to Fig. 8, in other examples, the pusher, instead of the previously shown wire 42, 542, can be an oversheath 242 that can be advanced over the outside of the microcatheter 212 and guided to advance the microvalve vessel occluder 230 to a designated longitudinal position relative to the distal end 216 of the microcatheter. The microvalve vessel occluder 230 can be attached to the oversheath 242 or alternatively abutted against the oversheath 242 without direct attachment. When directly attached, retraction of the microvalve vessel occluder is also permitted. The designated position may be at the distal end or an intermediate position over the microcatheter. Other aspects of the system are similar to as previously described.

[00119] Turning now to Figs. 9 through 11, in one method of use, the treatment system 10 (generally, but any of the systems described can likewise be used in accord with the following methods) can be used to inject a therapeutic agent into a target vessel 200 communicating with, for example, a solid tumor 202 of an organ. The tumor can be a cancerous tumor, such as a tumor specific to, for example, cancer of the pancreas, spleen, or small intestines. In addition, other non-cancerous diseased states of organs can also be treated using the systems and methods. In accord with the method, a guidewire 204 is advanced to a target location 206 in the target vessel 200 (Fig. 9). The microcatheter 12 is then advanced over the guidewire 204 so that its distal orifice 24 is at the target location 206 (Fig. 10). Then, the microvalve vessel occluder 30 is longitudinally displaced over the microcatheter 12 to the distal end of the microcatheter. In one example, radiographic imaging of the location of the markers 34 on the microvalve vessel occluder 30 relative to the distal marker 26 on the microcatheter 12 is used to determine when the microvalve vessel occluder is at the intended location at the distal end 16 of the microcatheter 12. The

guidewire 204 is removed from inside the microcatheter 12. Then, a therapeutic agent 208 is infused through the infusion lumen of the microcatheter 12, out of the distal orifice, and into the tumor 202 (Fig. 11). The microvalve vessel occluder 30 dynamically expands and contracts within a vessel 200 in relation to the surrounding fluid pressure in the vessel. In an example, the microvalve vessel occluder 30 may dynamically expand to a diameter between 0.5 mm and 20 mm. In an example, the microvalve vessel occluder 30 may dynamically expand to a diameter between 1.2 mm and 20 mm. In an example, the microvalve vessel occluder 30 may dynamically expand to a diameter between 1.2 mm and 10 mm. In an example, the microvalve vessel occluder 30 may dynamically expand to a diameter between 0.5 mm and 10 mm. When the therapeutic agent 208 is infused, the pressure in the vessel distal 210 of the treatment at times can be higher than that proximal 212 of the treatment, causing the microvalve vessel occluder 30 to open and block reflux of the therapeutic agent 208 to non-target areas. In addition, the microvalve vessel occluder 30 permits infusion into the tumor at high pressure, forcing the treatment deep into the target tissue 202. After the therapeutic agent 208 has been infused, the microvalve vessel occluder 30 and microcatheter 12 can be removed individually or together from the vessel 200 and the patient.

[00120] In other methods of use, the microvalve vessel occluder can be deployed in branching vessels to improve therapy delivery and uptake. In accord with one such method, a guidewire (not shown) is advanced to a target location 300 in a vessel 302 upstream of a one branched vessel 304 and distal of a second branched vessel 306 leading to target tissues 308, 310. Referring to Fig. 12, the microcatheter 12 is then advanced over the guidewire to the target location 300 (Fig. 12). Then, the microvalve vessel occluder 30 is longitudinally advanced over the microcatheter 12 to the distal end of the microcatheter. In one example, radiographic imaging of the location of the markers 34 on the microvalve vessel occluder 30 relative to the distal marker 26 on the microcatheter 12 is used to determine when the microvalve vessel occluder is at the intended location. The guidewire is removed from inside the microcatheter 12. Then, a therapeutic agent 312 is infused through the infusion lumen of the microcatheter 12, out of the distal orifice, and into the branched vessel 306 to the two target tissues 308, 310. The microvalve vessel occluder 30 dynamically expands and contracts within the vessel 302 in relation to the surrounding fluid pressure in the vessel. When the therapeutic agent 312 is infused, the pressure in the vessels distal 306 of the treatment at times can be higher than that upstream (proximal) 304 of the treatment, causing the microvalve vessel

occluder 30 to open and block reflux of the therapeutic agent 312 to the non-target upstream areas. After the therapeutic agent 312 has been infused, the microvalve vessel occluder 30 and microcatheter 12 can be removed individually or together from the vessel 302 and the patient.

[00121] Referring to Fig. 13, in another method of use within branching vessels, the microvalve vessel occluder is deployed over a microcatheter to define a primary treatment area, a secondary treatment area, and a non-treatment area. More particularly, a guidewire (not shown) is advanced to a target location 400 in a vessel 402. In one example, the target location has multiple distal branched vessels 404, and leads to a site of treatment delivery, such as a tumor 406. The microcatheter 12 is then advanced over the guidewire to the target location 400. Then, the microvalve vessel occluder 30 is longitudinally advanced over the microcatheter 12 to a location a selective distance from the distal end of the microcatheter, such that the microvalve vessel occluder is positioned proximal of the branched vessels 404. In this configuration, the distal tip 22 of the microcatheter 12 may, by way of example only, extend 5 to 60 mm beyond the microvalve vessel occluder 30. The guidewire is removed from inside the microcatheter 12. In one example, radiographic imaging of the location of the markers 34 on the microvalve vessel occluder 30 relative to the distal marker 26 on the microcatheter 12, in conjunction with imaging from contrast agent infusion through the microcatheter, is used to determine when the microvalve vessel occluder is at the intended location relative to the local anatomy. In one example, once the proper location is confirmed, a therapeutic agent 412 is infused through the infusion lumen of the microcatheter 12, out of the distal orifice of the microcatheter, and toward the primary treatment site 406. In addition, between the distal orifice and the microvalve vessel occluder, the microcatheter functions similarly to an end-hole catheter and may disperse therapeutic agent 412 in a lower concentration into the branched vessels 404. However, the microvalve vessel occluder 30 prevents non-targeted upstream delivery of the therapeutic agent upstream past the microvalve vessel occluder. As such, the microvalve vessel occluder 30 protects major areas, such as healthy tissues, from non-targeted delivery of therapeutic agents. After the therapeutic agent 412 has been infused, the microvalve vessel occluder 30 and microcatheter 12 can be removed individually or together from the vessel 402 and the patient.

[00122] Referring to Figs. 18 and 19, an exemplary treatment system 600 comprises a flexible guidewire 602 having a proximal end 604 and a distal end 606. A distal portion of the guidewire may be provided with one or more radiopaque marker bands. In an example, a first radiopaque

marker band 608 is provided adjacent a distal tip 610 of the guidewire 600. In an example, a plurality of radiopaque marker bands are provided along the distal portion of the guidewire 600 to aid in use of the system. In an example, a plurality of radiopaque markers are provided at the distal tip 610, on the distal end 606, on the proximal end 604, and/or between the proximal end 604 and the distal end 606. In an example, radiopaque marker bands are provided every 10 mm for a length of 60 mm from the distal tip 610 of the guidewire 602. In an example, radiopaque marker bands are provided every 10 mm for a length of 500 mm from the distal tip 610 of the guidewire 602. In an example, radiopaque marker bands are provided every 100 mm for a length of 500 mm from the distal tip 610 of the guidewire 602. In an example, radiopaque marker bands are provided every 50 mm for a length of 500 mm from the distal tip 610 of the guidewire 602.

[00123] Also referring to Figs. 18 and 19, an exemplary treatment system 600 comprises a flexible microcatheter 612 having a proximal end 614 and a distal end 616. A lumen extends along a longitudinal axis of the microcatheter 612 from the proximal end 614 to the distal end 616. The lumen opens to a distal orifice at the distal tip 618 of the microcatheter 612. A distal portion of the microcatheter 612 may be provided with one or more radiopaque marker bands. In an example, a first radiopaque marker band 620 may be provided adjacent a distal tip 618 of the microcatheter 612. In another example, a plurality of radiopaque markers are provided at the distal tip 618, on the distal end 616, on the proximal end 614, and/or between the proximal end 614 and the distal end 616. In a further example, a plurality of radiopaque marker bands are provided along the distal portion of the microcatheter 612. More specifically, each of the plurality of radiopaque marker bands are separated by a fixed distance along at least a portion of a length of the microcatheter 612. In an example, radiopaque marker bands are provided every 10 mm for a length of 60 mm from the distal tip 618 of the microcatheter 612. In another example, radiopaque marker bands are provided every 10 mm for a length of 500 mm from the distal tip 618 of the microcatheter 612. In a further example, radiopaque marker bands are provided every 100 mm for a length of 500 mm from the distal tip 618 of the microcatheter 612. In another further example, radiopaque marker bands are provided every 50 mm for a length of 500 mm from the distal tip 618 of the microcatheter 612.

[00124] Also referring to Figs. 18 and 19, an exemplary treatment system 600 of the present application comprises a catheter 622 having a proximal end 624 and a distal end 626. A lumen extends along a longitudinal axis of the catheter 622 from the proximal end 624 to the distal end

626. The lumen opens to a distal orifice at the distal tip 628 of the catheter 622. One or more radiopaque marker bands may be provided on a distal portion of the catheter 622. In an example, a first radiopaque marker band 630 may be provided adjacent a distal tip 638 of the catheter 622. In another example, a plurality of radiopaque markers are provided at the distal tip 628, on the distal end 626, on the proximal end 624, and/or between the proximal end 624 and the distal end 626. In a further example, a plurality of radiopaque marker bands are provided along the distal portion of the catheter 622. More specifically, each of the plurality of radiopaque marker bands are separated by a fixed distance along at least a portion of a length of the catheter 622. For example, radiopaque marker bands are provided every 10 mm for a length of 60 mm from the distal tip 628 of the catheter 622. In another example, radiopaque marker bands are provided every 10 mm for a length of 500 mm from the distal tip 628 of the catheter 622. In a further example, radiopaque marker bands are provided every 100 mm for a length of 500 mm from the distal tip 628 of the catheter 622. In a further example, radiopaque marker bands are provided every 50 mm for a length of 500 mm from the distal tip 628 of the catheter 622.

[00125] The catheter 622 comprises a microvalve vessel occluder 632 formed, attached, fixed, and/or connected to the catheter 622. In one example, the microvalve vessel occluder 632 is formed by attaching a first end of a braid of the microvalve vessel occluder 632 to the catheter 622, then everting the braid, and attaching a second end of the braid at a longitudinally displaced location on the catheter 622. The microvalve vessel occluder 632 is adapted to be self-expanding and dynamically move based on the relative fluid pressure conditions at opposing proximal and distal sides of the microvalve vessel occluder 632, in a substantially similar manner as microvalve vessel occluder 30 discussed above and illustrated in Fig. 1-17. For example, the microvalve vessel occluder 632 may comprise at least all of the features and details described above for a microvalve vessel occluder 30 discussed above and illustrated in Figs. 1-17.

[00126] In one example, the catheter 622 comprises an inner liner, an inner braid, and an outer coating. By way of example, the inner liner may be comprised of fluorinated polymer such as polytetrafluoroethylene (PTFE), fluorinated ethylene propylene (FEP), polypropylene, and/or polyethylene. By way of example, the inner liner may be chemically resistant. By way of example, the braid is comprised of metal such as stainless steel, nickel titanium alloy, tungsten, platinum, platinum iridium alloy, a polymer, polyethylene terephthalate (PET), and/or a liquid crystal polymer. By way of example, the braid may comprise reinforcing material. By way of example

the braid may comprise a coil of wire. By way of example, the outer coating is comprised of a thermoplastic elastomer, a polyether block amide thermoplastic elastomeric resin such as Pebax®, polyurethane, polyamide, copolymers of polyamide, polyester, copolymers of polyester, fluorinated polymers, such as PTFE, FEP, polyimides, polycarbonate, aromatic polyether and polyester such as Pellethane®, aliphatic polyether such as Tecoflex®, thermoplastic vulcanizates, ethylene propylene diene monomer rubber such as Santoprene®, silicone rubber another suitable material, any other standard material used in making catheters used in the bloodstream, and/or any other specialty material used in making catheters used in the bloodstream. By way of example, the catheter 622 comprises a hydrophilic coating on the outer coating, the hydrophilic coating may reduce friction and/or improve the trackability of the catheter 622. By way of example, the outer coating may comprise multiple segments of different materials along a length of the catheter 622. By way of example, the outer coating may comprise one or more softer materials distal to a stiffer material, one or more stiffer materials proximal to a softer material, and/or a stiffer material at the proximal end and a softer material at the distal end of the catheter 622.

[00127] The exemplary treatment system 600 may also comprise a sensing wire (not shown). The sensing wire comprises a proximal end and a distal end. The sensing wire may comprise one or more sensing elements. The one or more sensing elements of the sensing wire may be located at the proximal end, at the distal end, or therebetween the proximal end and the distal end of the sensing wire. Where the sensing wire comprises a plurality of sensing elements, the plurality of sensing elements may be grouped, clustered, and/or arranged. Where the sensing wire comprises a plurality of sensing elements, the plurality of sensing elements may be adjacent, near, at a fixed distance, and/or at different distances from the other sensing element and/or sensing elements. The sensing elements may, for example, be configured to measure one or more flow characteristics. In one example, a sensing element may measure a characteristic within the blood vessel, such as, for example, fluid pressure, vascular pressure, infusion pressure, flow rate, and/or infusion volume.

[00128] One or more radiopaque marker bands may be provided on a distal portion of the sensing wire. In one example, a first radiopaque marker band is provided adjacent to a distal tip of the sensing wire. In another example, a plurality of radiopaque markers are provided at the distal tip, on the distal end, on the proximal end, and/or between the proximal end and the distal end. In a further example, a plurality of radiopaque marker bands are provided along the distal portion of the sensing wire. More specifically, each of the plurality of radiopaque marker bands are separated

by a fixed distance along at least a portion of a length of the sensing wire. In an example, radiopaque marker bands are provided every 10 mm for a length of 60 mm from the distal tip of the sensing wire. In another example, radiopaque marker bands are provided every 10 mm for a length of 500 mm from the distal tip of the sensing wire. In a further example, radiopaque marker bands are provided every 100 mm for a length of 500 mm from the distal tip of the sensing wire. In another further example, radiopaque marker bands are provided every 50 mm for a length of 500 mm from the distal tip of the sensing wire.

[00129] In an example, the microcatheter 612 is configured for displacement relative to, and advancement over the guidewire 602 and/or sensing wire. In particular, the microcatheter 612 has a suitable length for the microcatheter 612 to be longitudinally displaced relative to the catheter 622 such that when the treatment system 600 is inserted into a target vessel and in place for infusion, the distal end of the microcatheter 612 is positioned at a target infusion location that is in fluid communications with a distal blood vessel that feeds a first volume of tissue less than (*e.g.*, at least 10% less, at least 20% less, at least 30% less, at least 40% less, at least 50% less, at least 60% less, at least 70% less, at least 80% less, at least 90% less, from at or about 10% to at or about 90% less, or from at or about 30% to at or about 80% less) a second volume of tissue that is fed by a distal blood vessel in fluid communications with a position of the microvalve vessel occluder 632 (*e.g.*, target occlusion location). In some examples, the microcatheter 612 can be longitudinally displaced relative to the catheter 622 such that when the treatment system 600 is inserted into a target vessel and in place for infusion, the microvalve vessel occluder 632 is positioned at a target occlusion location at least one bifurcation or at least two or more bifurcations (*e.g.*, two, three, four, five or six bifurcations, more particularly two or three) of branches upstream (*i.e.*, proximal) of the distal end of the microcatheter 612. In one example, the microcatheter 612 can be longitudinally displaced relative to the catheter 622 such that the microvalve vessel occluder 632 is proximal of the of the distal end of the microcatheter 612 by a length of about 20 cm or less, by about 15 cm or less, by about 10 cm or less. In particular, the microcatheter 612 can be longitudinally displaced relative to the catheter 622 such that the microvalve vessel occluder 632 is proximal of the of the distal end of the microcatheter 612 by a length from at or about 1 cm to at or about 20 cm, from at or about 1 cm to at or about 15 cm or less, or from at or about 1 cm to at or about 10 cm.

[00130] In a particular example, the microcatheter 612 has a length between two and eight feet

long. The length of the microcatheter 612 may correspond to the length of the guidewire 602 and/or sensing wire. The length of the microcatheter 612 may be less than 90% of the length of the guidewire 602 and/or sensing wire. The length of the microcatheter 612 may be at or about 90% of the length of the guidewire 602 and/or sensing wire. The length of the microcatheter 612 may be more than 90% of the length of the guidewire 602 and/or sensing wire. The length of the microcatheter 612 may be at or about 95% of the length of the guidewire 602 and/or sensing wire. The length of the microcatheter 612 may be at or about 98% of the length of the guidewire 602 and/or sensing wire.

[00131] In an example, the catheter 622 is configured for displacement relative to, and advancement over the microcatheter 612 and/or sensing wire. In a particular example, the catheter 622 has a length between two and eight feet long. The length of the catheter 622 may correspond to the length of the microcatheter 612 and/or sensing wire. The length of the catheter 622 may be less than 90% of the length of the microcatheter 612 and/or sensing wire. The length of the catheter 622 may be at or about 90% of the length of the microcatheter 612 and/or sensing wire. The length of the catheter 622 may be more than 90% of the length of the microcatheter 612 and/or sensing wire. The length of the catheter 622 may be at or about 95% of the length of the microcatheter 612 and/or sensing wire. The length of the catheter 622 may be at or about 98% of the length of the microcatheter 612 and/or sensing wire.

[00132] In an example, the guidewire 602 has an outer diameter of between 0.1 mm and 1.0 mm, between 0.2 mm and 1.0 mm, between 0.6 mm and 1.0 mm, between 0.7 mm and 1.0 mm, or between 0.8 mm and 1.0 mm. In another example, the guidewire 602 has an outer diameter of between 0.1 mm and 0.6 mm, between 0.1 mm and 0.7 mm, between 0.1 mm and 0.8 mm, or between 0.2 mm and 0.6 mm. In a further example, the guidewire 602 has an outer diameter of between 0.2 mm and 0.7 mm (corresponding to dimensional compatibility with the inner lumen diameter of catheter sizes 1.3 French to 2.8 French). In a further example, the guidewire 602 has an outer diameter of between 0.2 mm and 0.8 mm, or between 0.2 mm and 1.0 mm. The outer diameter of the guidewire 602 may be configured for movement, removal, advancement, and/or retraction through the microcatheter 612, catheter 622, the lumen of the catheter 622, a base catheter, and/or vasculature of a patient.

[00133] In an example, the sensing wire has an outer diameter of between 0.1 mm and 1.0 mm, between 0.2 mm and 1.0 mm, between 0.6 mm and 1.0 mm, between 0.7 mm and 1.0 mm, or

between 0.8 mm and 1.0 mm. In another example, the sensing wire has an outer diameter of between 0.1 mm and 0.6 mm, between 0.1 mm and 0.7 mm, between 0.1 mm and 0.8 mm, or between 0.2 mm and 0.6 mm. In a further example, the sensing wire has an outer diameter of between 0.2 mm and 0.7 mm (corresponding to dimensional compatibility with the inner lumen diameter of catheter sizes 1.3 French to 2.8 French). In a further example, the sensing wire has an outer diameter of between 0.2 mm and 0.8 mm, or between 0.2 mm and 1.0 mm. The outer diameter of the sensing wire may be configured for movement, removal, advancement, and/or retraction through the microcatheter 612, catheter 622, the lumen of the catheter 622, a base catheter, and/or vasculature of a patient.

[00134] In an example, the microcatheter 612 has an outer diameter of between 0.1 mm and 1.0 mm, or between 0.2 mm and 1.0 mm. In another example, the microcatheter 612 has an outer diameter of between 0.4 mm and 0.93 mm. In a further example, the microcatheter 612 has an outer diameter of between 1.3 French to 2.8 French. In a further example, the microcatheter 612 has an outer diameter of between 1.2 French to 2.8 French. In a further example, the microcatheter 612 has an outer diameter of between 0.6 mm and 1.0 mm, between 0.7 mm and 1.0 mm, or between 0.8 mm and 1.0 mm. In a further example, the microcatheter 612 has an outer diameter of between 0.1 mm and 0.6 mm. In a further example, the microcatheter 612 has an outer diameter of between 0.1 mm and 0.7 mm, between 0.1 mm and 0.8 mm, or between 0.2 mm and 0.6 mm. The outer diameter of the microcatheter 612 may be configured for movement, removal, advancement, and/or retraction through a catheter 622, a base catheter, and/or vasculature of a patient.

[00135] In an example, the microcatheter 612 has an inner diameter of between 0.1 mm and 1.0 mm, between 0.2 mm and 1.0 mm, between 0.6 mm and 1.0 mm, between 0.7 mm and 1.0 mm, or between 0.8 mm and 1.0 mm. In another example, the microcatheter 612 has an inner diameter of between 0.1 mm and 0.6 mm, between 0.1 mm and 0.7 mm, between 0.1 mm and 0.8 mm, or between 0.2 mm and 0.6 mm. In a further example, the microcatheter 612 has an inner diameter of between 0.2 mm and 0.7 mm (corresponding to catheter sizes 1.3 French to 2.8 French). In a further example, the microcatheter 612 has an inner diameter of between 0.2 mm and 0.8 mm, or between 0.2 mm and 1.0 mm. The inner diameter of the microcatheter 612 may be configured to allow for movement, removal, advancement, and/or retraction over the guidewire 602 and/or sensing wire.

[00136] The inner diameter of the microcatheter 612 may correspond to the outer diameter of the guidewire 602 and/or sensing wire. The inner diameter of the microcatheter 612 may be larger than the outer diameter of the guidewire 602 and/or sensing wire. The inner diameter of the microcatheter 612 may be one thousandth of an inch (.001") larger in diameter than the outer diameter of the guidewire 602 and/or sensing wire. The inner diameter of the microcatheter 612 may be thirty thousandths of an inch (.030") larger in diameter than the outer diameter of the guidewire 602 and/or sensing wire. The inner diameter of the microcatheter 612 may be between one thousandth of an inch and thirty thousandths of an inch (.001"- .030") larger in diameter than the outer diameter of the guidewire 602 and/or sensing wire. The inner diameter of the microcatheter 612 may be between two thousandths of an inch and twenty thousandths of an inch (.002"- .020") larger in diameter than the outer diameter of the guidewire 602 and/or sensing wire. The inner diameter of the microcatheter 612 may be between two thousandths of an inch and ten thousandths of an inch (.002"- .010") larger in diameter than the outer diameter of the guidewire 602 and/or sensing wire. The inner diameter of the microcatheter 612 may be configured to allow for the injection, delivery, infusion, flushing, and/or introduction of a therapeutic agent, contrast agent, saline, fluid, drug, and/or other material described herein.

[00137] In an example, the catheter 622 has an outer diameter of between 0.1 mm and 3.0 mm, between 0.2 mm and 3.0 mm, between 0.6 mm and 3.0 mm, between 0.7 mm and 3.0 mm, between 0.8 mm and 3.0 mm, or between 1.0 mm and 3.0 mm. In another example, the catheter 622 has an outer diameter of between 1.1176 mm and 1.4224 mm (corresponding to an outer diameter of between 0.044" and 0.056"). In a further example, the catheter 622 has an outer diameter of between 1.5 mm and 3.0 mm, between 1.8 mm and 3.0 mm, between 2.0 mm and 3.0 mm, between 2.5 mm and 3.0 mm, or between 2.8 mm and 3.0 mm. In a further example, the catheter 622 has an outer diameter of between 0.1 mm and 1.0 mm, between 0.1 mm and 1.5 mm, between 0.1 mm and 1.8 mm, between 0.1 mm and 2.0 mm, between 0.1 mm and 2.5 mm, or between 0.1 mm and 2.8 mm. In a further example, the catheter 622 has an outer diameter of between 0.7 mm and 1.0 mm, between 0.7 mm and 1.5 mm, or between 0.7 mm and 1.8 mm. In another example, the catheter 622 has an outer diameter of between 0.7 mm and 2 mm (corresponding to catheter sizes 2 French to 6 French). In a further example, the catheter 622 has an outer diameter of between 0.7 mm and 2.5 mm, between 0.7 mm and 2.8 mm, or between 0.7 mm and 3.0 mm. The outer diameter of the catheter 622 may be configured for movement, removal, advancement, and/or retraction

through a base catheter and/or vasculature of a patient. The outer diameter of the catheter 622 may be measured based on an outer surface of the catheter and the outer surface of the catheter may be rigid.

[00138] In an example, the catheter 622 has an inner diameter of between 0.1 mm and 2.5 mm, between 0.2 mm and 2.5 mm, between 0.4 mm and 2.5 mm, between 0.6 mm and 2.5 mm, between 0.7 mm and 2.5 mm, or between 0.8 mm and 2.5 mm. In another example, the catheter 622 has an inner diameter of between 0.889 mm and 0.9652 mm (corresponding to an inner diameter of between 0.035" and 0.038" and which is adapted for use with a microcatheter ranging from 1.3 French and 2.8 French in outer diameter). In a further example, the catheter 622 has an inner diameter of between 1.0 mm and 2.5 mm, between 1.5 mm and 2.5 mm, between 1.8 mm and 2.5 mm, or between 2.0 mm and 2.5 mm. In a further example, the catheter 622 has an inner diameter of between 0.1 mm and 0.4 mm, between 0.1 mm and 0.6 mm, between 0.1 mm and 0.7 mm, between 0.1 mm and 0.8 mm, between 0.1 mm and 1.5 mm, between 0.1 mm and 1.8 mm, or between 0.1 mm and 2.0 mm. In a further example, the catheter 622 has an inner diameter of between 0.4 mm and 0.6 mm, between 0.4 mm and 0.7 mm, between 0.4 mm and 0.8 mm, between 0.4 mm and 1.0 mm, or between 0.4 mm and 1.5 mm. In another example, the catheter 622 has an inner diameter of between 0.4 mm and 1.8 mm (corresponding to catheter sizes 2 French to 6 French). In a further example, the catheter 622 has an inner diameter of between 0.4 mm and 2.0 mm, or between 0.4 mm and 2.5 mm. The inner diameter of the catheter 622 may be configured to allow for movement, removal, advancement, and/or retraction over the microcatheter 612, guidewire 602, and/or sensing wire.

[00139] The inner diameter of the catheter 622 may correspond to the outer diameter of the microcatheter 612 and/or sensing wire. The inner diameter of the catheter 622 may be larger than the outer diameter of the microcatheter 612 and/or sensing wire. The inner diameter of the catheter 622 may be one thousandth of an inch (.001") larger in diameter than the outer diameter of the microcatheter 612 and/or sensing wire. The inner diameter of the catheter 622 may be forty thousandths of an inch (.040") larger in diameter than the outer diameter of the microcatheter 612 and/or sensing wire. The inner diameter of the catheter 622 may be between one thousandth of an inch and forty thousandths of an inch (.001"- .040") larger in diameter than the outer diameter of the microcatheter 612 and/or sensing wire. The inner diameter of the catheter 622 may be between two thousandths of an inch and twenty thousandths of an inch (.002"- .020") larger in diameter than

the outer diameter of the microcatheter 612 and/or sensing wire. The inner diameter of the catheter 622 may be between two thousandths of an inch and ten thousandths of an inch (.002"-.010") larger in diameter than the outer diameter of the microcatheter 612 and/or sensing wire. The inner diameter of the catheter 622 may be configured to allow for the injection, delivery, infusion, flushing, and/or introduction of a therapeutic agent, contrast agent, saline, fluid, drug, and/or other material described.

[00140] A base catheter may be used for the introduction of any of the described treatment systems. The base catheter may comprise an inner diameter and an outer diameter. The outer diameter of the base catheter may be configured for movement, removal, advancement, and/or retraction through the vasculature of a patient. The inner diameter of the base catheter may be configured to allow for movement, removal, advancement, and/or retraction of a guidewire 602, sensing wire, microcatheter 612, and/or catheter 622. In an example, the base catheter has an outer diameter of between 1.2 mm and 7.0 mm, between 1.2 mm and 5.0 mm, between 1.2 mm and 4.0 mm, between 1.5 mm and 7.0 mm, between 1.5 mm and 5.0 mm, or between 1.5 mm and 4.0 mm. In another example, the base catheter has an outer diameter of between 4.0 mm and 7.0 mm, between 5.0 mm and 7.0 mm, or between 1.2 mm and 1.5 mm.

[00141] Referring to Fig. 20, an exemplary treatment system 700 may be used in with the treatment system 600 of Figs. 18 and 19, the treatment system 700 comprises a hub 702. The hub 702 may be attached to a proximal end 704 of the catheter 706. The hub 702 may comprise a first port 708 configured to allow a microcatheter 710, guidewire (not shown), and/or sensing wire (not shown) to move, advance, and/or retract through a lumen of the catheter 706. The first port 708 of the hub 702 may be concentrically aligned with the lumen of the catheter 706. The first port of the hub 702 may be configured to allow for the injection, delivery, infusion, flushing, and/or introduction of a fluid (*e.g.*, an infusate), comprising, for example, a therapeutic agent, contrast agent, saline, drug, and/or other material described herein. The hub 702 may comprise a second port 712 which may extend at an angle from a longitudinal axis of the catheter 706. The second port 712 may be configured to allow for the injection, delivery, infusion, flushing, and/or introduction of a fluid (*e.g.*, an infusate) comprising, for example, a therapeutic agent, contrast agent, saline, drug, and/or other material described herein. The second port 712 may be configured to allow for the injection, delivery, infusion, flushing, and/or introduction of a fluid (*e.g.*, an infusate) comprising, for example, a therapeutic agent, contrast agent, saline, drug, and/or other

material described herein through the lumen of the catheter 706. The second port 712 may be configured to allow for the injection, delivery, infusion, flushing, and/or introduction of a fluid (e.g., an infusate) comprising, for example, a therapeutic agent, contrast agent, saline, drug, and/or other material described herein through the lumen of the catheter 706, while the microcatheter 710, guidewire, and/or sensing wire are within the lumen of the catheter 706. The hub 702 may, for example comprise, a hemostasis valve.

[00142] Fig. 26 shows another example of a treatment system 2600 for delivering a fluid (e.g., an infusate) into a target vessel in fluid communication with, for example, a solid tumor of an organ. The treatment system 2600 is substantially similar to the treatment system 600 shown in Fig. 18 and 19, except as otherwise noted below. The exemplary treatment system 2600 comprises a first tubular element 2602 (e.g., a catheter or a portion of a catheter), an occluder 2622 attached to the first tubular element 2602, and a second tubular element 2662. The treatment system 2600 also comprises a hub 2642 mounted to a proximal portion of the first tubular element 2602, and a hub 2682 mounted to a proximal portion of the second tubular element 2662. The first tubular element 2602 extends from a proximal end 2604 to a distal end 2606 and comprises an outer surface 2608, a lumen 2610 extending from a proximal orifice located at the proximal end 2604 to a distal orifice 2612 located at the distal end 2606, and an inner surface along the lumen 2610. The occluder 2622 is attached to a distal portion of the first tubular element 2602, and further comprises a proximal end 2624, and a distal end 2626. The occluder 2622 is attached to the outer surface 2608 of the first tubular element 2602 via a proximal attachment 2628 and a distal attachment 2630. The distal attachment 2630 may, for example, be located at the distal end 2606 of the first tubular element 2602 and/or at a distance proximal to the distal end 2606 of the first tubular element 2602. The proximal attachment 2628 may, for example, be located at a distance proximal to the distal attachment 2630 and/or at a distance proximal to the distal end 2606 of the first tubular element 2602.

[00143] The hub 2642 is mounted to a proximal portion or a proximal end 2604 of the first tubular element 2602. The hub 2642 comprises a proximal end 2644 and a distal end 2646. The second tubular element 2662 comprises a proximal end 2664, a distal end 2666, an outer surface 2668, a lumen extending from a proximal orifice located at the proximal end 2664 to a distal orifice 2670 located at the distal end 2666, and an inner surface along the lumen. The hub 2682 is mounted to a proximal portion or a proximal end 2664 of the second tubular element 2662. The hub 2682

comprises a proximal end 2684 and a distal end 2686.

[00144] The first tubular element 2602, second tubular element 2662, and occluder 2622 may, for example, be concentrically aligned. In other words, the first tubular element 2602, the second tubular element 2662 and the occluder 2622 may be co-axial along a common longitudinal axis. The first tubular element 2602, second tubular element 2662, and/or occluder 2622 may, for example, be sized to be longitudinally displaceable and/or rotationally moveable relative to one another. In particular, the first tubular element 2602 is longitudinally displaceable and/or rotationally moveable relative to the second tubular element 2662 such that the occluder 2622 is longitudinally displaceable and/or rotationally movable relative to the second tubular element 2662. A diameter of the lumen 2610 of the first tubular element 2602 is larger than a diameter of the outer surface 2668 of the second tubular element 2662. When a portion of the second tubular element 2662 is located within the lumen 2610 of the first tubular element 2602, an inter-catheter space between the outer surface 2668 of the second tubular element 2662 and the inner surface of the first tubular element 2602 is formed. In one example, the first tubular element 2602 is a catheter.

[00145] The second tubular element 2662 may be a microcatheter configured for delivering a fluid (*e.g.*, an infusate) to a target vessel. As shown in Fig. 26, the second tubular element 2662 may be longer than the first tubular element 2602. The second tubular element 2662 extends along a length from the proximal end 2664 to the distal end 2666. In particular, the second tubular element 2662 has a suitable length for the second tubular element 2662 to be longitudinally displaced relative to first tubular element 2602 such that when the treatment system 2600 is inserted into a target vessel and in place for infusion, the distal end of the second tubular element 2662 is positioned at a target infusion location that is in fluid communications with a distal (*i.e.*, downstream in arteries and upstream in veins) blood vessel that feeds a first volume of tissue less than (*e.g.*, at least 10% less, at least 20% less, at least 30% less, at least 40% less, at least 50% less, at least 60% less, at least 70% less, at least 80% less, at least 90% less, from at or about 10% to at or about 90% less, or from at or about 30% to at or about 80% less) a second volume of tissue that is fed by a distal blood vessel in fluid communications with a position of the occluder 2622 (*e.g.*, target occlusion location). In some examples, the second tubular element 2662 can be longitudinally displaced relative to the first tubular element 2602 such that when the treatment system 2600 is inserted into a target vessel and in place for infusion, the occluder 2622 is

positioned at a target occlusion location at least one bifurcation or at least two or more bifurcations (*e.g.*, two, three, four, five, or six bifurcations, more particularly, two or three) of branches upstream (*i.e.*, proximal) of the distal end 2666 of the second tubular element 2662. In one example, the second tubular element 2662 can be longitudinally displaced relative to the first tubular element 2602 such that the occluder 2622 is proximal of the of the distal end 2666 of the second tubular element 2662 by a length of about 20 cm or less, by about 15 cm or less, by about 10 cm or less. In particular, the second tubular element 2662 can be longitudinally displaced relative to the first tubular element 2602 such that the occluder 2622 is proximal of the of the distal end 2666 of the second tubular element 2662 by a length from at or about 1 cm to at or about 20 cm, from at or about 1 cm to at or about 15 cm or less, or from at or about 1 cm to at or about 10 cm. The length from the proximal end 2664 to the distal end 2666 of the second tubular element 2662 may be, for example, from at or about 60 cm to at or about 200 cm.

[00146] The outer surface 2668 of the second tubular element 2662 has a cross-sectional diameter that is substantially consistent or consistent throughout the length of the second tubular element 2662. The diameter of the outer surface 2668 of the second tubular element 2662 may be, for example, from at or about 0.5 mm to at or about 3 mm. In another example, the diameter of the outer surface 2668 of the second tubular element 2662 may be from at or about 1.5 French to at or about 9 French. The second tubular element 2662 may, for example, comprise an inner liner, an inner braid, and/or an outer coating, each similar to those describe above with respect to microcatheter 12 and catheter 622.

[00147] The second tubular element 2662 may, for example, comprise one or more radiopaque marker bands similar to the radiopaque marker bands described above with respect to Figs. 18 and 19. The second tubular element 2662 may, for example, comprise a first radiopaque marker band located adjacent to the distal end 2666 of the second tubular element 2662, a second radiopaque marker band located a fixed distance (*e.g.*, at or about 10 mm) proximal to a first radiopaque marker band located adjacent to the distal end 2666 of the second tubular element 2662. In another example, the second tubular element 2662 may comprise a plurality of radiopaque marker bands that are separated by a fixed distance along at least a portion of a length of the second tubular element 226, for example, a plurality of radiopaque marker bands spaced 10 millimeters from one or more adjacent radiopaque marker bands proximally from a first radiopaque marker band located adjacent to the distal end 2666 of the second tubular element 2662.

[00148] The occluder 2622 may be a microvalve vessel occluder. The microvalve vessel occluder comprises a filamentary structure comprising a plurality of filamentary strands, such as, for example, a braided filamentary structure 2632 and a fluid impermeable polymeric membrane and/or a porous polymeric filter 2634 covering at least a portion of (*i.e.*, a portion of or completely covering) the occluder 2622. The fluid impermeable polymeric membrane and/or a porous polymeric filter 2634 may, for example, coat a proximal portion of the occluder 2622, a central portion of the occluder 2622, and/or a distal portion of the occluder 2622. The fluid impermeable polymeric membrane and/or a porous polymeric filter construct 2634 may, for example, extend between and across the one or more filaments of the filamentary structure 2632. In one example, the occluder 2622 is similar to the microvalve vessel occluder 30 described above and constructed from a tubular braid of multiple strands in tubular form and coated with a fluid impermeable polymeric membrane or a porous polymeric filter construct.

[00149] Referring to Fig. 27, another exemplary treatment system 2700 for delivering a fluid (e.g., an infusate) into a target vessel in fluid communication with, for example, a solid tumor of an organ is shown. The exemplary treatment system 2700 comprises a first tubular element 2702, a second tubular element 2762, and an occluder 2782 attached to a distal portion of the second tubular element 2762. The treatment system 2700 may further comprise a hub 2722 mounted to a proximal portion of the first tubular element 2702. The first tubular element 2702 extends from a proximal end 2704 to a distal end 2706 and comprises an outer surface 2708, a lumen extending from a proximal orifice located at the proximal end 2704 to a distal orifice 2710 located at the distal end 2706, and an inner surface along the lumen. The hub 2722 is mounted to a proximal portion or a proximal end 2704 of the first tubular element 2702. The hub 2722 comprises a proximal end 2724 and a distal end 2726. The second tubular element 2762 extends from a proximal end 2764 to a distal end 2766 and comprises an outer surface 2768, a lumen extending from a proximal orifice located at the proximal end 2764 to a distal orifice located at the distal end 2766, and an inner surface along the lumen. The occluder 2782 is attached to a distal portion of the second tubular element 2762, and further comprises a proximal end 2784 and a distal end 2786. The occluder 2787 is attached to the outer surface 2768 of the second tubular element 2762 via a proximal attachment and a distal attachment. The distal attachment may, for example, be located at the distal end 2766 of the second tubular element 2762 and/or at a desired distance proximal to the distal end 2766 of the second tubular element 2762. The proximal attachment may, for

example, be located at a proximal end 2764 of the second tubular element 2762, at another desired distance proximal to the distal attachment and/or at a further desired distance proximal to the distal end 2766 of the second tubular element 2762.

[00150] The second tubular element 2762 may be a short tubular structure (the term ‘short’ as defined above). The second tubular element 2762 extends along a length from the proximal end 2764 to the distal end 2766. The length from the proximal end 2764 to the distal end 2766 of the second tubular element 2762 may be, for example, at or about 2 mm, at or about 10 mm, at or about 20 mm, or at or about 200 mm. In another example, the length of the second tubular element 2762 may be, for example from at or about 2 mm to at or about 10 mm, from at or about 2 mm to at or about 20 mm, or from at or about 2 mm to at or about 200 mm.

[00151] The second tubular element 2762 may be formed of an elastic material such that a cross-sectional diameter of the lumen of the second tubular element 2762 is radially expandable. The diameter of the lumen of the second tubular element 2762 in a relaxed, unexpanded configuration may be, for example, at or about 0.3 mm, at or about 3 mm, or at or about 6 mm. In some examples, the diameter of the lumen diameter of the second tubular element 2762 in a relaxed, unexpanded configuration may be from at or about 0.3 mm to at or about 3 mm, or from at or about 0.3 mm to at or about 6 mm. In some examples, the diameter of the lumen of the second tubular element 2762 is elastically expandable to at or about 120%, at or about 200%, or at or about 400% of the diameter in a relaxed, unexpanded configuration. In another example, the diameter of the lumen of the second tubular element 2762 is elastically expandable to between at or about 120% and at or about 200%, between at or about 120% and at or about 400% of the diameter in a relaxed, unexpanded configuration.

[00152] The second tubular element 2762 may be flexible and elastic material such that a cross-sectional diameter of the lumen of the second tubular element 2762 is radially expandable. The second tubular element 2762 may be formed from a flexible and elastic material such as an elastic polymer. The second tubular element 2762 may, for example, be formed from or comprise one or more fluorinated polymers. The second tubular element 2762 may, for example, be formed from or comprise one or more polyether block amide thermoplastic elastomeric resins. The second tubular element 2762 may, for example, be formed from or comprise Pebax®, polyurethane, polyamide, copolymers of polyamide, polyester, copolymers of polyester, fluorinated polymers, polytetrafluoroethylene (PTFE), fluorinated ethylene propylene (FEP), polyimides, polycarbonate,

rubber, synthetic rubber, and/or silicone rubber.

[00153] The first tubular element 2702, second tubular element 2762, and/or occluder 2782 may, for example, be concentrically aligned. In other words, the first tubular element 2702, second tubular element 2762 and/or the occluder 2782 may be co-axial along a common longitudinal axis. The first tubular element 2702 and the second tubular element 2762 may, for example, be sized to be longitudinally displaceable and/or rotationally moveable relative to one another. In particular, the second tubular element 2762 is longitudinally displaceable and/or rotationally moveable relative to first tubular element 2702 such that the occluder 2784 is longitudinally displaceable and/or rotationally movable relative to the first tubular element 2702. The occluder 2782 may be longitudinally displaced relative to the first tubular element 2702 by the same lengths as discussed above with respect to displacement of microvalve vessel occluder 30 over a microcatheter.

[00154] The first tubular element 2702 may be a catheter. A diameter of the lumen of the second tubular element 2762 is larger than a diameter of the outer surface 2708 of the first tubular element 2702. In another example, a diameter of the lumen of the second tubular element 2762 is equal or substantially equal to the diameter of the outer surface 2708 of the first tubular element 2702. In one example, a diameter of the lumen of the second tubular element 2762 in a relaxed, unexpanded configuration may have a smaller diameter than the diameter of the outer surface 2708 of the first tubular element 2702 such that the second tubular element 2762 is at least partially expanded when placed over the outer surface 2708 to provide a frictional fit of the second tubular element 2762 onto the outer surface 2708 of the first tubular element 2702.

[00155] The frictional fit may, for example, maintain the relative longitudinal positioning between the first tubular element 2702 with the second tubular element 2762 and the occluder 2782. The frictional fit may, for example, maintain the relative longitudinal positioning between the first tubular element 2702 and the second tubular element 2762 when the first tubular element 2702 is advanced distally into or retracted proximally from the vasculature of the patient. The frictional fit may, for example, maintain the relative longitudinal positioning between the first tubular element 2702 and the second tubular element 2762 until a longitudinal force that is sufficient to overcome the frictional fit is applied between the first tubular element 2702 and the second tubular element 2762. A longitudinal force for overcoming the frictional fit may be applied in either a proximal-to- distal or a distal-to-proximal direction. The longitudinal force may be at least 0.5 Newton, at least 1 Newton, at least 4.9 Newton, at least 5 Newton, at least 9.8 Newton,

at least 10 Newton, at least 14.7 Newton, at least 15 Newton, at least 19.6 Newton, and/or at least 20 Newton.

[00156] In another example, the diameter of the lumen of the second tubular element 2762 in a relaxed, unexpanded configuration may have a larger diameter than the diameter of the outer surface 2708 of the first tubular element 2702. For example, the second tubular element 2762 may be temporarily affixed onto the outer surface 2708 of the first tubular element 2702 with an adhesive such that the relative longitudinal positioning between the first tubular element 2702 and the second tubular element 2762 is maintained when the first tubular element 2702 is advanced distally into or retracted proximally from the vasculature of the patient. The adhesive maintains the relative longitudinal positioning between the first tubular element 2702 and the second tubular element 2762 until a longitudinal force that is sufficient to overcome the adhesive is applied between the first tubular element 2702 and the second tubular element 2762.

[00157] The occluder 2782 may be a microvalve vessel occluder. The microvalve vessel occluder comprises a filamentary structure comprising a plurality of filamentary strands, such as, for example, a braided filamentary structure and a fluid impermeable polymeric membrane and/or a porous polymeric filter covering at least a portion of (*i.e.*, a portion of or completely covering) the occluder 2782. The fluid impermeable polymeric membrane and/or a porous polymeric filter may, for example, coat a proximal portion of the occluder 2782, a central portion of the occluder 2782, and/or a distal portion of the occluder 2782. The fluid impermeable polymeric membrane and/or a porous polymeric filter construct may, for example, extend between and across the one or more filaments of the filamentary structure.

[00158] In an example, a plurality of markings or radiopaque marker bands are provided along a distal portion or an entire length of the first tubular element 2702 to aid in determining a position of the occluder 2782 relative to the first tubular element 2702. In one example, markings or radiopaque marker bands are provided every 1 cm, every 0.5 cm, or every 1 mm. The markings or radiopaque markers may be provided for the entire length of the first tubular element 2702. Alternatively, the markings or radiopaque markers may be provided for a length (*e.g.*, from at or about 1 mm to at or about 500 mm) from the distal end 2706 of the first tubular element 2702).

[00159] Referring to Figs. 28A and 28B, another example of a treatment system 2800 for delivering a fluid (*e.g.*, an infusate) into a target vessel in fluid communication with, for example, a solid tumor of an organ is shown. The exemplary treatment system 2800 comprises a first tubular

element 2802 (*e.g.*, a catheter), a first occluder portion 2822 attached to the first tubular element 2802, a second tubular element 2862, and a second occluder portion 2882 attached to the second tubular element 2862. The first tubular element 2802 extends from a proximal end 2804 to a distal end 2806 and comprises an outer surface 2808, a lumen extending from a proximal orifice located at the proximal end 2804 to a distal orifice located at the distal end 2806, an inner surface along the lumen, and wall between the inner surface and the outer surface 2808. The first occluder portion 2822 is attached to a distal portion of the first tubular element 2802, and further comprises a proximal end 2824, and a distal end 2826. The second tubular element 2862 extends from a proximal end 2864 to a distal end 2866, and further comprises an outer surface 2868, a lumen extending from a proximal orifice located at the proximal end 2864 to a distal orifice 2872 located at the distal end 2866, and an inner surface along the lumen. The second occluder portion 2882 is attached to a distal portion of the second tubular element 2862, and further comprises a proximal end 2884 and a distal end 2886. The second occluder portion 2882 is attached to the outer surface 2868 of the second tubular element 2862 via an attachment 2888.

[00160] The treatment system 2800 may also comprise a hub 2842 mounted a proximal portion of to the first tubular element 2802 and a hub 2892 mounted a proximal portion of to the second tubular element 2862. The treatment system 2800 may further comprise a handle (not shown). The hub 2842 is mounted to a proximal portion or a proximal end 2804 of the first tubular element 2802. The hub 2842 comprises a proximal end 2844 and a distal end 2846. The hub 2842 is attached at the proximal end 2844 to a luer lock coupling 2848 (*e.g.*, for attaching syringes, tubing, etc.), and a hemostasis element (*e.g.*, hemostasis valve) 2850. In one example, the hub 2842, the luer lock coupling 2848 and the hemostasis element 2850 may be formed as a single unit. The hub 2892 mounted to a proximal portion or a proximal end 2864 of the second tubular element 2862. The hub 2842 comprises a proximal end 2894, a distal end 2896, and a first port 2898.

[00161] The first tubular element 2802 and the second tubular element 2862 may, for example, be concentrically aligned. In other words, the first tubular element 2802 and the second tubular element 2866 may be co-axial along a common longitudinal axis. The first tubular element 2802, the first occluder portion 2822, second tubular element 2862, and/or second occluder portion 2882 may, for example, be sized to be longitudinally displaceable and/or rotationally moveable relative to one another. In particular, the first tubular element 2802 is rotationally moveable relative to the second tubular element 2866 such that the first occluder portion 2822 attached to the first tubular

element 2802 is rotationally moveable relative to the second occluder portion 2882 of attached to the second tubular element 2862. For example, the first occluder portion 2822 may be rotationally moveable relative to the second occluder 2882 to modulate the level of occlusion of the target vessel provided at the target occlusion location, modulate flow of fluids past the first and second occluder portions 2822, 2882 and/or modulate a pressure distal (*i.e.*, downstream in arteries and upstream in veins) of the first and second occluder portions 2822, 2882. A diameter of the lumen of the first tubular element 2802 is larger than a diameter of the outer surface 2868 of the second tubular element 2862 such that the second tubular member 2862 is longitudinally displaceable relative to the first tubular element 2802 within the lumen of the first tubular element 2862. When a portion of the second tubular element 2862 is located within the lumen of the first tubular element 2802, an inter-catheter space between the outer surface 2868 of the second tubular element 2862 and the inner surface of the first tubular element 2802 is formed.

[00162] The first tubular element 2802 may, for example, be a catheter configured for insertion into a target vessel. In one example, the first tubular element 2802 may be a catheter or a hypotube comprising an inner liner, an inner braid and an outer coating similar to microcatheter 12 describe above with respect to Figs. 1 and 2 and the catheter 622 described above with respect to Figs. 18 and 19, unless otherwise noted below. The first tubular element 2802 may, for example, comprise a hypotube having an inner liner and/or an outer coating. The first tubular element 2802 extends along a length from the proximal end 2804 to the distal end 2806. The length from the proximal end 2804 to the distal end 2806 of the first tubular element 2802 may be, for example, from at or about 40 cm to at or about 180 cm. The outer surface 2808 of the first tubular element 2802 has a cross-sectional diameter that is substantially consistent or consistent throughout the length of the first tubular element 2802. The diameter of the outer surface 2808 of the first tubular element 2802 may be, for example, from at or about 1 mm to at or about 3 mm. In another example, the diameter of the outer surface 2808 of the first tubular element 2802 may be from at or about 3 French to at or about 9 French.

[00163] The wall of the first tubular element 2802 between the outer surface 2808 and the inner surface of the first tubular element 2802 may have a substantially uniform thickness throughout the length of the first tubular element 2802. The thickness of the wall of the first tubular element 2802 may be, for example, at or about 0.05 mm, at or about 0.1 mm, at or about 0.15 mm, or at or about 0.25mm. In another example, the thickness of the wall of the first tubular element 2802 may

from at or about 0.05 mm to at or about 0.1mm, from at or about 0.05 mm to at or about 0.15 mm, from at or about 0.05 mm or at or about 0.25mm, or from at or about 0.1 mm or at or about 0.15mm.

[00164] The second tubular element 2862 may, for example, be a catheter configured for delivering a fluid (*e.g.*, an infusate) to a target vessel. In one example, the second tubular element 2862 may be a catheter or a hypotube comprising an inner liner, an inner braid and an outer coating similar to microcatheter 12 describe above with respect to Figs. 1 and 2 and the catheter 622 described above with respect to Figs. 18 and 19, unless otherwise noted below. The second tubular element 2862 extends along a length from the proximal end 2864 to the distal end 2866. As shown in Fig. 28A, the second tubular element 2862 may be longer than the first tubular element 2802. The outer surface 2868 of the second tubular element 2862 has a cross-sectional diameter that is substantially consistent or consistent throughout the length of the second tubular element 2662. The diameter of the outer surface 2868 of the second tubular element 2862 may be, for example, from at or about 0.5 mm to at or about 3 mm. In another example, the diameter of the outer surface 2868 may be from at or about 1.5 French to at or about 9 French. The second tubular element 2862 may, for example, comprise a inner liner, a braid, and/or an outer coating, each similar to those describe above with respect to microcatheter 12 and catheter 622.

[00165] Additionally, the lumen of the second tubular element 2862 is configured to receive a third tubular element (not shown) therethrough. The third tubular element may be a microcatheter configured for delivering a fluid (*e.g.*, an infusate) to a target vessel similar to the second tubular element 2862 discussed above. The second tubular element 2862 and the third tubular element may, for example, be concentrically aligned. In other words, the second tubular element 2862 and the third tubular element may be co-axial along a common longitudinal axis. The second tubular element 2862 and the third tubular element, may, for example, be sized to be longitudinally displaceable and/or rotationally moveable relative to one another. A diameter of the lumen of the second tubular element 2862 is larger than a diameter of an outer surface of the third tubular element. The first and second occluder portions 2822, 2882 can be longitudinally displaced relative the third tubular element by the same lengths as discussed above with respect to displacement of occluder 2622 over the second tubular element 2662.

[00166] The first occluder portion 2822 attached to the first tubular element 2802 may, for example, comprise one or more flexible structure(s) that conform to a diameter of a target vessel when it is inserted and in use for occluding the blood vessel. In particular, flexible structure(s)

extend radially from the first tubular element 2802. For example, the first tubular element 2802 may comprise one or more elastic leaflets for occluding a blood vessel. The elastic leaflet may comprise a plurality of supporting filaments coated with a fluid permeable polymer filter material or a fluid impermeable polymer membrane. The supporting filaments may be metal (e.g., stainless steel or nickel-titanium alloy) filaments or standards, or polymer filaments or strands. The fluid permeable polymer filter material or fluid impermeable polymer membrane extends across the plurality of support filaments and may cover in part or completely the elastic leaflet. In one example, the flexible structure comprises linearly or spirally arranged filaments extending radially around a diameter of the first tubular element 2802. When the one or more flexible structure(s) are introduced to a blood vessel, the filaments symmetrically deflect and conform to an inner lumen of the blood vessel. In some examples, the filaments symmetrically deflect and conform to an inner lumen having a diameter from at or about 0.5 mm to at or about 8 mm, or from at or about 0.5 mm to at or about 5 mm.

[00167] Similarly, the second occluder portion 2882 attached to the second tubular element 2862 may, for example, comprise one or more flexible structure(s) that conform to a diameter of a target vessel when it is inserted and in use for occluding the blood vessel. In particular, the flexible structure(s) extend radially from the second tubular element 2862. The flexible structure(s) of the second occluder portion 2882 may be similar to the structures described above for the first occluder portion 2822.

[00168] In another embodiment, the first occluder portion 2822 attached to the first tubular element 2802 may, for example, comprise one or more balloon occluder(s). The balloon occluder(s) are each movable between an inflated configuration, in which an interior cavity of the balloon occluder is filled with a fluid and a deflated configuration in which fluid is withdrawn from the interior cavity of the balloon occluder. As shown in the example of Fig. 28A and 28B, the balloon occluder(s) of the first occluder portion 2822 are attached to the first tubular element 2802 along the same cross-sectional plane and about the longitudinal axis of the first tubular element 2802. The first occluder portion 2822 attached to the first tubular element 2802 comprises a first balloon occluder and a second balloon occluder. The balloon occluder(s) of the first occluder portion 2822 may be arranged in an occluder pattern, such as, for example, a symmetrical arrangement or an asymmetrical arrangement.

[00169] In this embodiment, the second occluder portion 2882 attached to the second tubular

element 2862 similarly comprises one or more balloon occluder(s). The balloon occluder(s) are each movable between an inflated configuration, in which an interior cavity of the balloon occluder is filled with a fluid and a deflated configuration in which fluid is withdrawn from the interior cavity of the balloon occluder. As shown in the example of Fig. 28A and 28B, the balloon occluder(s) of the second occluder portion 2882 are attached to the second tubular element 2862 along the same cross-sectional plane and about the longitudinal axis of the first tubular element 2802. The second occluder portion 2882 attached to the second tubular element 2862 comprises a first balloon occluder and a second balloon occluder. The balloon occluder(s) of the second occluder portion 2882 may be arranged in an occluder pattern, such as, for example, a symmetrical arrangement or an asymmetrical arrangement.

[00170] The occluder pattern of the first occluder portion 2822 and the occluder pattern of the second occluder portion 2882 together may form a composite occluder pattern arrangement, where the occluder pattern of the first occluder portion 2822 is complementary to the occluder pattern of the second occluder portion 2882. The occluder pattern of the first occluder portion 2822 and the occluder pattern of the second occluder portion 2882 may be the same or different. In one example, the composite occluder pattern comprises a symmetrical occluder pattern for the first occluder portion 2822 and a same or different symmetrical occluder pattern for the second occluder portion 2882. Each of the occluder patterns for the first and second occluder portions 2822, 2882 may be, for example, one of the five patterns shown in Fig. 28C. The handle may comprise any suitable mechanism for actuating longitudinal and/or rotational movement of the first tubular element 2802 and the first occluder portion 2822 relative to the second tubular element 2862 and the second occluder portion 2882, and *vice versa*. For example, the handle may comprise a mechanism (*e.g.*, a rotational knob) for controlling rotational movement of the first tubular element 2802 relative to the second tubular element 2862, or *vice versa*. The handle may also comprise any suitable mechanism for inflating and/or deflating each of the balloon occluders of the first and second occluder portion 2822, 2882.

[00171] Referring to Fig. 29, another example of a treatment system 2900 for delivering a fluid (*e.g.*, an infusate) into a target vessel in fluid communication with, for example, a solid tumor of an organ is shown. The exemplary treatment system 2900 comprises a first tubular element 2902, an occluder 2922 attached to the first tubular element 2902, and a second tubular element 2942. The first tubular element 2902 extends along a length from a proximal end 2904 to a distal end

2906. The first tubular element 2902 further comprises an outer surface 2908, a lumen 2912 extending from a proximal orifice located at the proximal end 2904 to a distal orifice located at the distal end 2906, and an inner surface 2910 along the lumen 2912. The occluder 2922 is attached to and surrounds a portion of the first tubular element 2902, as shown in Fig. 29.

[00172] In one example, the occluder 2922 is a balloon occluder. The balloon occluder may, for example, have a spherical shape, a disc shape, an ellipsoidal shape, and/or a geometry that provides an atraumatic surface when in contact and/or in partial contact with a blood vessel of a patient. The occluder 2922 comprises a proximal end 2924, and a distal end 2926. The proximal end 2924 of the occluder 2922 is attached to the first tubular element 2902 via a proximal attachment 2928, and the distal end 2926 of the occluder 2922 is attached to the first tubular element 2902 via a distal attachment 2930. The occluder 2922 further comprises one or more occluder port(s) 2932, each of which extends through a wall of the first tubular element 2902 and is in fluid communication with an interior cavity 2934 of the occluder 2922. The second tubular element 2942 extends along a length from a proximal end 2944 to a distal end 2946. The second tubular element 2942 further comprises an outer surface 2948, a lumen 2952 extending from a proximal orifice located at the proximal end 2944 to a distal orifice 2954 located at the distal end 2946, and an inner surface 2950 along the lumen 2952. The first tubular element 2902, second tubular element 2942, and occluder 2922 may, for example, be concentrically aligned. In other words, the first tubular element 2902, second tubular element 2942, and occluder 2922 may be co-axial along a common longitudinal axis.

[00173] The first tubular element 2902 may be a catheter. The distal end 2906 of the first tubular element 2902 is sealed with a distal seal 2918 around the second tubular element 2942. The distal seal 2918 is attached to the inner surface 2910 of the first tubular element 2902 and provides a fluid tight seal that prevents fluid from exiting the distal end 2906 of the first tubular element 2902. The distal seal 2918 may comprise a structural seal, a sealing agent, a gasket, or may be in the form of a narrowing of a diameter of the inner lumen of the first tubular element 2902 to create a fluid tight seal.

[00174] In one embodiment, the second tubular element 2942 may have a cross-sectional diameter that is substantially consistent or consistent throughout the length of the second tubular element 2942. Optionally, the second tubular element 2942 may, for example, be a tapered microcatheter. In one example, a distal tip of the second tubular element 2942 is tapered to

facilitate insertion through the distal seal 2918. In another example, the tapered microcatheter comprises a proximal portion, a distal portion and a tapered portion fluidly connecting the proximal portion to the distal portion. The distal portion has a distal outer diameter smaller than a proximal outer diameter of the proximal portion. The tapered portion has a proximal end connected to the proximal portion and a distal end connected to the distal portion. The proximal portion and the tapered portion may have any suitable length for inserting through the distal seal 2948. The outer diameter of the proximal end of the tapered portion is the same as the proximal outer diameter of the proximal portion. Similarly, the outer diameter of the distal end of the tapered portion is the same as the distal outer diameter of the distal portion. In some examples, the second tubular element 2942 has an inner diameter that is consistent or substantially consistent throughout the proximal portion, the distal portion and the tapered portion.

[00175] As shown in Fig. 29, the distal seal 2918 of the first tubular element 2902 is sufficiently tight on a proximal portion second tubular element 2942 so that it forms a fluid tight seal. The second tubular element 2942 is longitudinally displaceable relative to the first tubular element 2902 through the distal seal 2918. The distal seal 2918 maintains the fluid tight seal as the second tubular element 2942 is longitudinally displaced relative to the first tubular element 2902. The occluder 2922 may be longitudinally displaced relative to the second tubular element 2942 by the same lengths as discussed above with respect to displacement of microvalve vessel occluder 30 over a microcatheter.

[00176] When a portion of the second tubular element 2942 is located within the lumen 2912 of the first tubular element 2902 an inter-catheter space between the outer surface 2948 of the second tubular element 2942 and the inner surface 2910 of the first tubular element 2902 is formed. When a fluid is injected into the inter-catheter space between the second tubular element 2942 and the first tubular element 2902 and into the occluder 2922 through the occluder port 2932, the fluid exits the inter-catheter space via the one or more occluder port(s) 2932 and thereby filling the occluder 2922 and causing it to expand. Therefore, infusion of fluid into the inter-catheter space inflates the occluder 2922 and withdrawal of fluid from the inter-catheter space deflates the the occluder 2922.

[00177] Fig. 30 shows another example of a treatment system 3000 for delivering a fluid (e.g., an infusate) into a target vessel in fluid communication with, for example, a solid tumor of an organ. The exemplary treatment system 3000 comprises a first tubular element 3002, a second

tubular element 3022 and an occluder 3082. The first tubular element 3002 extends from a proximal end 3004 to a distal end 3006 and comprise an outer surface 3008, a lumen 3010 extending from a proximal orifice located at the proximal end 3004 to a distal orifice located at the distal end 3006, an inner surface along the lumen 3010, a wall between the inner surface and the outer surface 3008. The second tubular element 3022 extends from a proximal end 3024 to a distal end 3026, and comprises an outer surface, a lumen 3028 extending from a proximal orifice located at the proximal end 3024 to a distal orifice 3030 located at the distal end 3026, and an inner surface along the lumen 3028. The occluder 3082 is attached to a distal portion of the first tubular element 3002 and a distal portion of the second tubular element 3022, and further comprises a proximal end and a distal end. The occluder 3082 is attached to the first tubular element 3002 via a first attachment 3088 and to the second tubular element 3022 via a second attachment 3090. The first attachment 3088 to the first tubular element 3002 may, for example, be at the distal end 3006 of the first tubular element 3002 and/or at the a distance proximal to the distal end 3006 of the first tubular element 3002. The second attachment 3090 to the second tubular element 3022 may, for example, be at the distal end 3026 of the second tubular element 3022 and/or at the a distance proximal to the distal end 3026 of the second tubular element 3022.

[00178] The treatment system 3000 also comprises a hub 3042 mounted to a distal portion of the second tubular element 3022 and a handle 3062. The hub 3042 is mounted to a proximal portion or a proximal end 3024 of the second tubular element 3022 comprises a proximal end 3044, a distal end 3046, and a first port 3048. The handle 3062 comprises mechanisms for controlling the longitudinal and/or rotational movement of a first tubular element 3002 and/or a second tubular element 3022. For example, the handle 3062 may comprise a slider assembly, such as for example, a spool and shaft, the combination of which converts manual longitudinal movement of a user manipulating the handle 3062 into a longitudinal displacement of the first tubular element 3002 and/or the second tubular element 3022. In another example, the handle 3062 may comprise a rotation knob connected to a lead screw that converts manual user rotational movement into a longitudinal displacement between the distal ends of the first tubular element 3002 and/or the second tubular element 3022. In a further example, the handle 3062 may comprise a rotational knob for controlling rotational movement of the first tubular element 3002 relative to the second tubular element 3022, or *vice versa*. The handle 3062 may also comprise mechanisms for controlling and/or filling the occluder 3082.

[00179] The first tubular element 3002 and the second tubular element 3022 may, for example, be concentrically aligned. In other words, the first tubular element 3002 and the second tubular element 3022 may be co-axial along a common longitudinal axis. The first tubular element 3002 and the second tubular element 3022 may, for example, be sized to be longitudinally displaceable and/or rotationally moveable relative to one another. A diameter of the lumen of the first tubular element 3002 is larger than a diameter of the outer surface of the second tubular element 3022. When a portion of the second tubular element 3022 is located within the lumen of the first tubular element 3010, an inter-catheter space between the outer surface of the second tubular element 3022 and the inner surface of the first tubular element 3002 is formed.

[00180] The first tubular element 3002 may be catheter. The first tubular element 3002 may, for example comprise an inner liner, an inner braid, and/or an outer coating each similar to those described above with respect to microcatheter 12 and catheter 622. In some examples, the first tubular element 3002 extends a length from the proximal end 3004 to the distal end 3006 from at or about 40 cm to at or about 180 cm. The outer surface 3008 of the first tubular element 3002 may have a diameter from at or about 1 mm to at or about 3 mm. In another example, the diameter of the outer surface 3008 of the first tubular element 3002 may be from at or about 3 French to at or about 9 French. The thickness of the wall of the first tubular element 3002 may, for example, be at or about 0.05 mm, at or about 0.1 mm, at or about 0.15 mm, or at or about 0.25 mm. In another example, the thickness of the wall of the first tubular element 3002 may be from at or about 0.05 mm to at or about 0.1 mm, from at or about 0.05 mm to at or about 0.15 mm, from at or about 0.05 mm to at or about 0.25 mm, or from at or about 0.1 mm to at or about 0.15 mm.

[00181] The second tubular element 3022 comprises a catheter substantially similar to the first tubular element 3002, except as noted below. The second tubular element 3022 extends a length from the proximal end 3024 to the distal end 3026. The length of the second tubular element 3022 may, for example, be from at or about 40 cm to at or about 160 cm. The outer surface of the second tubular element 3022 may, for example, have a diameter from at or about 0.5 mm to at or about 3 mm. In another example, the diameter of the outer surface of the second tubular element 3022 may be from at or about 1.5 French to at or about 9 French.

[00182] The occluder 3082 comprises a compliant membrane containing an occluder fill material. The compliant membrane of the occluder 3082 may, for example, be comprised of one or more elastic materials, such as, for example, one or more silicone materials, one or more

polyurethane rubber materials, one or more polyether block amide materials, and/or one or more thermoplastic elastomer materials. The occluder fill material may, for example, be comprised of a fluid, a gel, an incompressible fluid, a semi-fluid, water, a saline solution, a silicone oil, a silicone gel, and/or a hydrogel.

[00183] The longitudinal displacement of the first tubular element 3002 relative to the second tubular element 3022 expands or contracts a diameter of the occluder 3082 to increase or decrease amount of occlusion in the target vessel provided by the occluder 3082, respectively. For example, the distance between the first attachment 3088 on the first tubular element 3002 relative to a second attachment 3090 on the second tubular element 3022 may, for example, correspond to a compressive force and/or a tensile force applied to the compliant membrane and/or the occluder fill material to expand or contract a diameter of the occluder 3082. A smaller distance between the first attachment 3088 and the second attachment 3090 corresponds to a greater compressive force and/or a lesser tensile force that results in expansion of the diameter of the occluder 3082. A larger distance between the first attachment 3088 and the second attachment 3090 corresponds to a greater tensile force and/or a lesser compressive force that result in contraction of the diameter of the occluder 3082.

[00184] Additionally, the lumen 3028 of the second tubular element 3022 is configured to receive a third tubular element (not shown) therethrough. The third tubular element may be a microcatheter configured for delivering a fluid (*e.g.*, an infusate) to a target vessel similar to the third tubular element discussed above with respect to treatment system 2800. The second tubular element 3022 and the third tubular element may, for example, be concentrically aligned. In other words, the second tubular element 3022 and the third tubular element may be co-axial along a common longitudinal axis. The second tubular element 3022 and the third tubular element, may, for example, be sized to be longitudinally displaceable and/or rotationally moveable relative to one another. A diameter of the lumen of the second tubular element 3022 is larger than a diameter of an outer surface of the third tubular element. The occluder 3082 can be longitudinally displaced relative to the third tubular element by the same lengths as discussed above with respect to displacement of occluder 2622 over the second tubular element 2662.

[00185] Fig. 31 shows another example of a treatment system 3100 for delivering a fluid (*e.g.*, an infusate) into a target vessel in fluid communication with, for example, a solid tumor of an

organ. Fig. 31 is substantially similar to Fig. 30 described above, with like components being numbered with like reference numerals, except as noted below.

[00186] The occluder 3182 comprises a filamentary structure comprising a plurality of filamentary strands in parallel and a fluid impermeable polymeric membrane and/or a porous polymeric filter covering at least a portion of (*i.e.*, a portion of or completely covering) the occluder 3182. The filamentary structure may, for example, be comprised of one or more filaments. The filaments may, for example, extend from a first attachment 3188 on the first tubular element 3102 to a second attachment 3190 on the second tubular element 3122. For example, the filaments are fused to or otherwise fixedly coupled to the first tubular element 3102 and the second tubular element 3122 at the first attachment 3188 and the second attachment 3190, respectively. The filaments may, for example, extend concentrically around the first tubular element 3102 and/or the second tubular element 3122. The filaments may, for example, be comprised of a metal, a flexible metal, a shape memory material, and/or a polymer. The filaments may, for example, be comprised of a stainless steel, a nickel-titanium alloy, a PET, a polyethylene-naphthalate (PEN), a liquid crystal polymer, a fluorinated polymer, a nylon, a polyamide and/or any other suitable polymer. The occluder 3182 may, for example, be comprised of a filter or a mesh of elastic material such as fluid permeable polymer filter material or fluid impermeable polymer membrane such as, for example, the polymer coatings described in U.S. Pat. Nos. 8,696,698, 9,968,740, 10,588,636 and/or US Serial No. 17/969,506. The fluid impermeable polymeric membrane and/or the porous polymeric filter may, for example, cover a proximal portion of the occluder 3182, a central portion of the occluder 3182, and/or a distal portion of the occluder 3182. The fluid impermeable polymeric membrane and/or a porous polymeric filter may, for example, extend between and across the one or more filaments of the filamentary structure. The first attachment 3188 to the first tubular element 3102 may, for example, be located at the distal end 3106 of the first tubular element 3102 and/or at a distance proximal to the distal end 3106 of the first tubular element 3102. The second attachment 3190 to the second tubular element 3122 may, for example, be located at the distal end 3126 of the second tubular element 3122 and/or at a distance proximal to the distal end 3126 of the second tubular element 3122.

[00187] The longitudinal displacement of the first tubular element 3102 relative to the second tubular element 3122 expands or contracts a diameter of the occluder 3182 to increase or decrease amount of occlusion in the target vessel provided by the occluder 3182, respectively. For example,

the distance between the first attachment 3188 on the first tubular element 3102 relative to a second attachment 3190 on the second tubular element 3122 may, for example, correspond to a compressive force and/or a tensile force applied to the filamentary structure to expand or contract a diameter of the occluder 3182. A smaller distance between the first attachment 3188 and the second attachment 3190 corresponds to a greater compressive force and/or a lesser tensile force that results in expansion of the diameter of the occluder 3182. A larger distance between the first attachment 3188 of the occluder 3182 and the second attachment 3190 of the occluder 3182 corresponds to a greater tensile force and/or a lesser compressive force that result in contraction of the diameter of the occluder 3182.

[00188] Additionally, the lumen of the second tubular element 3122 comprises a lumen extending therethrough configured to receive a third tubular element (not shown) there through. The third tubular element may be a microcatheter configured for delivering a fluid (*e.g.*, an infusate) to a target vessel similar to the third tubular element discussed above with respect to treatment system 2800. The second tubular element 3122 and the third tubular element may, for example, be concentrically aligned. In other words, the second tubular element 3122 and the third tubular element may be co-axial along a common longitudinal axis. The second tubular element 3122 and the third tubular element, may, for example, be sized to be longitudinally displaceable and/or rotationally moveable relative to one another. A diameter of the lumen of the second tubular element 3122 is larger than a diameter of an outer surface of the third tubular element. The occluder 3182 can be longitudinally displaced relative the third tubular element by the same lengths as discussed above with respect to displacement of occluder 2622 over the second tubular element 2662.

[00189] Fig. 32 shows another example of a treatment system 3200 for delivering a fluid (*e.g.*, an infusate) into a target vessel in fluid communication with, for example, a solid tumor of an organ. Fig. 32 is substantially similar to Figs. 30 and 31 described above, with like components being numbered with like reference numerals, except as noted below.

[00190] The occluder 3282 comprises a tubular braid filamentary structure comprising a plurality of filamentary strands braided with each other, and a fluid impermeable polymeric membrane and/or a porous polymeric filter covering at least a portion of (*i.e.*, a portion of or completely covering) the occluder 3282. The tubular braid structure may, for example, be comprised of one or more filaments. The filaments may, for example, extend from a first

attachment 3288 on the first tubular element 3202 to a second attachment 3290 on the second tubular element 3222. For example, the filaments are fused to or otherwise fixedly coupled to the first tubular element 3202 and the second tubular element 3222 at the first attachment 3288 and the second attachment 3190, respectively. The filaments in a configuration may, for example, extend concentrically around the first tubular element 3202 and/or the second tubular element 3222. The filaments may, for example, be comprised of a metal, a flexible metal, a shape memory material, and/or a polymer. The filaments may, for example, be comprised of a stainless steel, a nickel-titanium alloy, a PET, a polyethylene-naphthalate (PEN), a liquid crystal polymer, a fluorinated polymer, a nylon, a polyamide and/or any other suitable polymer. The occluder 3282 may, for example, be comprised of a filter or a mesh of elastic material such as fluid permeable polymer filter material or fluid impermeable polymer membrane such as, for example, the polymer coatings described in U.S. Pat. Nos. 8,696,698, 9,968,740, 10,588,636 and/or US Serial No. 17/969,506. The fluid impermeable polymeric membrane and/or the porous polymeric filter may, for example, cover a proximal portion of the occluder 3182, a central portion of the occluder 3182, and/or a distal portion of the occluder 3182. The fluid impermeable polymeric membrane and/or a porous polymeric filter construct may, for example, extend between and across one or more filaments of the tubular braid structure. The first attachment 3288 to the first tubular element 3202 may, for example, be located at the distal end 3206 of the first tubular element 3202 and/or at a distance proximal to the distal end 3206 of the first tubular element 3202. The second attachment 3290 to the second tubular element 3222 may, for example, be located at the distal end 3226 of the second tubular element 3222 and/or at a distance proximal to the distal end 3226 of the second tubular element 3222.

[00191] The longitudinal displacement of the first tubular element 3202 relative to the second tubular element 3222 expands or contracts a diameter of the occluder 3282 to increase or decrease amount of occlusion in the target vessel provided by the occluder, 3282, respectively. For example, the distance between the first attachment 3288 on the first tubular element 3202 relative to the second attachment 3290 on the second tubular element 3222 may, for example, correspond to a compressive force and/or a tensile force applied to the tubular braid structure to expand or contract a diameter of the occluder 3282. A smaller distance between the first attachment 3288 and the second attachment 3290 corresponds to a greater compressive force and/or a lesser tensile force and an expanded configuration that results in expansion of the diameter of the occluder 3282.

A larger distance between the first attachment 3288 and the second attachment 3290 corresponds to a greater tensile force and/or a lesser compressive force that result in contraction of the diameter of the occluder 3282.

[00192] Additionally, the second tubular element 3222 comprises a lumen extending therethrough configure to receive a third tubular element (not shown) there through. The third tubular element may be a microcatheter configured for delivering a fluid (*e.g.*, an infusate) to a target vessel similar to the third tubular element discussed above with respect to treatment system 2800. The second tubular element 3222 and the third tubular element may, for example, be concentrically aligned. In other words, the second tubular element 3222 and the third tubular element may be co-axial along a common longitudinal axis. The second tubular element 3222 and the third tubular element, may, for example, be sized to be longitudinally displaceable and/or rotationally moveable relative to one another. A diameter of the lumen of the second tubular element 3222 is larger than a diameter of an outer surface of the third tubular element. The occluder 3282 can be longitudinally displaced relative to the third tubular element by the same lengths as discussed above with respect to displacement of occluder 2622 over the second tubular element 2662.

[00193] Referring to Figure 33, another exemplary treatment system 3300 for delivering a fluid (*e.g.*, an infusate) into a target vessel in fluid communication with, for example, a solid tumor of an organ is shown. The exemplary treatment system 3300 comprises a first tubular element 3302, a second tubular element 3322, and an occluder 3382. The first tubular element 3302 extends from a proximal end 3304 to a distal end 3306, and comprises an outer surface 3308, a lumen 3310 extending from a proximal orifice located at the proximal end 3304 to the distal end 3306, an inner surface along the lumen 3310, and a wall between the inner surface and the outer surface 3308. The second tubular element 3322 extends from a proximal end 3324 to a distal end 3326, and comprises an outer surface, a lumen 3328 extending from a proximal orifice located at the proximal end 3324 to a distal orifice 3330 located at the distal end 3326, and an inner surface along the lumen 3328.

[00194] The treatment system 3300 also comprise a hub 3342 mounted to the second tubular element 3322, a handle 3362, and one or more wires. The hub 3342 is mounted to a proximal portion or a proximal end 3326 of the second tubular element 3322. The hub 3342 comprises a proximal end 3344, a distal end 3346, and a first port 3348. The handle 3362 further comprises

mechanisms for controlling the longitudinal movement of a first tubular element 3302 and/or a second tubular element 3322. For example, the handle 3362 may comprise a slider assembly, such as, for example, a spool and shaft, the combination of which converts manual longitudinal movement of a user manipulating the handle 3362 into a longitudinal displacement of the first tubular element 3302 and/or the second tubular element 3322. In another example, the handle 3362 may comprise a rotation knob connected to a lead screw that converts manual user rotational movement into a longitudinal displacement between the distal ends of the first tubular element 3302 and/or the second tubular element 3322. The occluder 3382 further comprises a proximal end and a distal end, and is attached to the first tubular element 3302 via a proximal attachment 3388, and a distal attachment 3390. The distal attachment 3390 may, for example, be located at the distal end 3306 of the first tubular element 3302 and/or at a distance proximal to the distal end 3306 of the first tubular element 3302. The proximal attachment 3388 may, for example, be located at a distance proximal to the distal attachment 3390 and/or at a distance proximal to the distal end 3306 of the first tubular element 3302. The first tubular element 3302 and the second tubular element 3322 may, for example, be concentrically aligned. In other words, the first tubular element 3302 and the second tubular element 3322 may be co-axial along a common longitudinal axis. The distal end 3306 of the first tubular element 3302 may, for example, be coupled to the proximal end 3324 of the second tubular element 3322. A diameter of the lumen 3310 of the first tubular element 3302 may, for example, be larger than, smaller than, and/or equal to a diameter of the outer surface of the second tubular element 3322. The coupling between the distal end 3306 of the first tubular element 3302 and the proximal end 3324 of the second tubular element 3322 is configured to allow a therapeutic agent to move in a proximal-to-distal direction and/or in a distal-to-proximal direction between the lumen 3310 of the first tubular element 3302 and the lumen 3328 of the second tubular element 3322, the distal orifice 3330 of the second tubular element 3322, the distal end 3326 of the second tubular element 3322, and a location distal to the distal end 3326 of the second tubular element 3322.

[00195] The first tubular element 3302 may be a catheter. The first tubular element 3302 may, for example, comprise an inner liner, an inner braid, and/or an outer coating each similar to those described above with respect to microcatheter 12 and catheter 622. In some examples, the first tubular element 3302 extends a length from the proximal end 3304 to the distal end 3306 from at or about 40 cm to at or about 180 cm. The outer surface 3308 of the first tubular element 3302

may have a diameter from at or about 1 mm to at or about 3 mm. In another example, the diameter of the outer surface 3308 of the first tubular element 3302 may be from at or about 3 French to at or about 9 French. The thickness of the wall of the first tubular element 3302 may, for example, be at or about 0.05 mm, at or about 0.1 mm, at or about 0.15 mm, or at or about 0.25 mm. In another example, the thickness of the wall of the first tubular element 3302 may be from at or about 0.05 mm to at or about 0.1 mm, from at or about 0.05 mm to at or about 0.15 mm, from at or about 0.05 mm to at or about 0.25 mm, or from at or about 0.1 mm to at or about 0.15 mm.

[00196] The second tubular element 3322 comprises an extendible tubular member that is movable between an extended length and a retracted length. The extendible tubular element may, for example, comprise a coil reinforced structure. The coil reinforced structure may, for example, be comprised of one or more coiled filaments. The second tubular element 3322 extends from the proximal end 3324 to the distal end 3326 to an extended length from at or about 1 cm to at or about 20 cm. The outer surface of the second tubular element 3322 has a diameter that expands when the length of the second tubular element 3322 is retracted and contracts when the length of the second tubular element 332 is extended. The second tubular element 3322 may, for example, comprise a inner liner, a braid, and/or an outer coating each similar to those described above with respect to microcatheter 12 and catheter 622.

[00197] The one or more wires are coupled connect to the second tubular element 3322 to articulate an extension or retraction of the length of the second tubular element 3322. The one or more wires may, for example, be coupled to the second tubular element 3322 to articulate changes the length of the second tubular element 3322. The one or more wires may, for example, be coupled to the distal end 3326 of the second tubular element 3322 to change a length of the second tubular element 3322.

[00198] The occluder 3382 is a microvalve vessel occluder. In one example, the microvalve vessel occluder 632 is adapted to be self-expanding and dynamically move based on the relative fluid pressure conditions at opposing proximal and distal sides of the microvalve vessel occluder 3382, in a substantially similar manner as microvalve vessel occluder 30 discussed above and illustrated in Fig. 1-17. For example, the microvalve vessel occluder 632 may comprise at least all of the features and details described above for a microvalve vessel occluder 30 discussed above and illustrated in Figs. 1-17.

[00199] The handle 3362 may, for example, modify a position and/or a configuration of one or

more of the first tubular element 3302, the second tubular element 3322, the occluder 3382, the hub 3342 mounted to the second tubular element 3322, and/or the one or more wires. The handle 3362 may, for example, modify a position of the first tubular element 3302 relative to the second tubular element 3322. The handle 3362 may, for example, modify a position of the second tubular element 3322 relative to the first tubular element 3302. The handle 3362 may, for example, modify a position of the one or more wires. The handle may, for example, comprise a rotation knob. The rotation knob may, for example, be configured to convert rotational movement of the rotation knob to modify a position and/or a configuration of one or more of the first tubular element 3302, the second tubular element 3322, the occluder 3382, the hub 3342 mounted to the second tubular element 3322, and/or the one or more wires. The handle may, for example, comprise a slider assembly. The slider assembly may, for example, be configured to convert movement of the handle to modify a position and/or configuration of one or more of the first tubular element 3302, the second tubular element 3322, the occluder 3382, the hub 3342 mounted to the second tubular element 3322, and/or the one or more wires. The handle may, for example, comprise a spool and shaft. The spool and shaft may, for example, be configured to convert movement of the handle to modify a position and/or configuration of one or more of the first tubular element 3302, the second tubular element 3322, the occluder 3382, the hub 3342 mounted to the second tubular element 3322, and/or the one or more wires.

[00200] Fig. 34 shows another example of a treatment system 3400 for delivering a fluid (e.g., an infusate) into a target vessel in fluid communication with, for example, a solid tumor of an organ. Fig. 34 is substantially similar to Fig. 33 described above, with like components being numbered with like reference numerals, except as noted below.

[00201] The first tubular element 3402, second tubular element 3482, and/or occluder 3422 may, for example, be sized to be longitudinally displaceable and/or rotationally displaceable relative to one another. A diameter of the lumen 3410 of the first tubular element 3402 is larger than a diameter of the outer surface 3488 of the second tubular element 3482. When a portion of the second tubular element 3482 is located within the lumen 3410 of the first tubular element 3402 an inter-catheter space between the outer surface 3488 of the second tubular element 3482 and the inner surface of the first tubular element 3402 is formed.

[00202] The thickness of the wall of the first tubular element 3402 may, for example, be at or about 0.05 mm, at or about 0.1 mm, at or about 0.15 mm, or at or about 0.25 mm. In additional

examples, the thickness of the wall of the first tubular element 3402 may be from at or about 0.05 mm to at or about 0.1 mm, from at or about 0.05 mm to at or about 0.15 mm, from at or about 0.05 mm to at or about 0.25 mm, or from at or about 0.1 mm to at or about 0.15 mm. The first tubular element 3402 may, for example, comprise one or more channels and/or one or more wire lumens. The one or more channels and/or one or more flexible wire lumens are configured to allow one or more wires to pass therethrough. The one or more channels and/or one or more flexible wire lumens are configured to allow one or more wires to connect to the second tubular element 3482.

[00203] The second tubular element 3482 is a short catheter (the term 'short' as defined above). The second tubular element 3482 extends a length from the proximal end 3484 to the distal end 3486. The length of the second tubular element 3482 may, for example, be from at or about 2 cm to at or about 30cm. The length of the second tubular element 3482 may, for example, be shorter than the length of the first tubular element 3402. The length of the second tubular element 3482 may, for example, be at or about 1%, at or about 10%, at or about 25%, at or about 50%, at or about 75%, or at or about 90% of the length of the first tubular element 3402. In another example, the length of the second tubular element 3482 may be from at or about 1% to at or about 10%, from at or about 1 to at or about 25%, from at or about 1% to at or about 50%, from at or about 1% to at or about 75%, or from at or about 1% to at or about 90% of the length of the first tubular element 3402. The diameter of the outer surface 3488 of the second tubular element 3402 may, for example, be smaller than a diameter of a lumen of the first tubular element 3402. The diameter of the outer surface 3488 of the second tubular element 3402 may, for example, be from at or about 0.0005 inches to at or about 0.020 inches smaller than the diameter of the lumen of the first tubular element 3402.

[00204] The one or more wires may, for example, be coupled to the second tubular element 3482 to move the second tubular element 3482 in a proximal-to-distal and/or a distal-to-proximal direction. The one or more wires may, for example, be coupled to the proximal end 3484 and/or the distal end 3486 of the second tubular element 3482 to move the second tubular element 3482 in a proximal-to-distal and/or a distal-to-proximal direction.

[00205] The second tubular element 3482 may further comprise one or more radiopaque marker bands. The second tubular element 3482 may, for example, comprise a first radiopaque marker band located adjacent to the distal end 3486 of the second tubular element 3482, a second radiopaque marker band located proximal to a first radiopaque marker band, and/or a plurality of

radiopaque marker bands spaced from one or more adjacent radiopaque marker bands.

[00206] The handle 3462 may, for example, modify a position and/or a configuration of one or more of the first tubular element 3402, the second tubular element 3482, the occluder 3422, the hub 3442 mounted to the first tubular element 3402, and/or the one or more wires. The handle 3462 may, for example, modify a position of the first tubular element 3402 relative to the second tubular element 3482. The handle 3462 may, for example, modify a position of the second tubular element 3482 relative to the first tubular element 3402. The handle 3462 may, for example, be configured to modify a configuration of the occluder. The handle 3462 may, for example, be configured to modify a location of the second tubular element 3482. The handle 3462 may, for example, modify a position of the one or more wires. The handle may, for example, comprise a rotation knob. The rotation knob may, for example, be configured to convert rotational movement of the rotation knob to modify a position and/or a configuration of one or more of the first tubular element 3402, the second tubular element 3482, the occluder 3422, the hub 3442 mounted to the first tubular element 3402, and/or the one or more wires. The handle may, for example, comprise a slider assembly. The slider assembly may, for example, be configured to convert movement of the handle to modify a position and/or configuration of one or more of the first tubular element 3402, the second tubular element 3482, the occluder 3422, the hub 3442 mounted to the first tubular element 3402, and/or the one or more wires. The handle may, for example, comprise a spool and shaft. The spool and shaft may, for example, be configured to convert movement of the handle to modify a position and/or configuration of one or more of the first tubular element 3402, the second tubular element 3482, the occluder 3422, the hub 3442 mounted to the first tubular element 3402, and/or the one or more wires.

[00207] Turning to Figs. 21A through 21D, exemplary configurations for a treatment system in an exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient are shown. The treatment systems discussed above, in particular, treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel 800 in fluid communication with, for example, a solid tumor 802 of an organ according to the method illustrated by Figs. 21A through 21D discussed herein. As shown in Fig. 21A, a microcatheter 804 may be moved, in particular, advanced distally into the vasculature, until a distal end of the microcatheter 804 reaches a target infusion location. Then, as shown in Fig. 21B, a

tubular member, such as, for example, a catheter 806 comprising a microvalve vessel occluder 808 (such as, for example, the catheter 622 comprising a microvalve vessel occluder 632 described above) may be moved, in particular, advanced distally into the vasculature, over the microcatheter 804 through a distal opening (also referred to herein as a distal orifice) of a lumen of the tubular member (*e.g.*, catheter) 806, until a distal end of the tubular member (*e.g.*, catheter) 806 and/or the microvalve vessel occluder 808 reaches a target occlusion location. The target infusion location may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) to of the target occlusion location of the distal end of the tubular member (*e.g.*, catheter) 806. Then, as shown in Fig. 21C, a fluid (*e.g.*, an infusate) comprising a therapeutic agent 810 may be delivered through the distal opening of the lumen of the microcatheter 804 causing the microvalve vessel occluder 808 to expand when vascular pressure distal to the microvalve vessel occluder 808 exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder 808. Then, the microcatheter 804 may be removed (*i.e.*, withdrawn) from the target vessel 800 through the lumen of the tubular member (*e.g.*, catheter) 806. Then, as shown in Fig. 21D, the lumen of the tubular member (*e.g.*, catheter) 806 may be flushed with contrast and/or saline 812. Flushing the lumen of the tubular member (*e.g.*, catheter) 806 with contrast and/or saline 812 may generate higher pressure within the vasculature distal to the microvalve vessel occluder 808 and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor 802.

[00208] Turning to Figs. 22A through 22D, exemplary configurations for a treatment system in an exemplary method of delivering a therapeutic agent within a vasculature of a patient are shown. The treatment systems discussed above, in particular, treatment systems 10, 600 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel 900 in fluid communication with, for example, a solid tumor 902 of an organ according to the method illustrated by Figs. 22A through 22D discussed herein. Figs. 22A-22C are substantially the same as Figs. 21A-22C described above, with like components being numbered with like reference numerals. As shown in Fig. 22A, a microcatheter 904 may be moved until a distal end of the microcatheter 904 reaches a target infusion location. Then, as shown in Fig. 22B, a tubular member (*e.g.*, catheter) 906 comprising a microvalve vessel occluder 908 may be moved over the microcatheter 904 through a distal opening of a lumen of the tubular member (*e.g.*, catheter) 906 until a distal end of the tubular member (*e.g.*,

catheter) 906 and/or the microvalve vessel occluder 908 reaches a target occlusion location. Then, as shown in Fig. 22C, therapeutic agent 910 may be delivered through the distal opening of the lumen of the microcatheter 904 causing the microvalve vessel occluder 908 to expand when vascular pressure distal to the microvalve vessel occluder 908 exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder 908. Then, as shown in Fig. 22D, a distal end of a sensing wire 912 may then be moved to a sensing location within the vasculature of the patient. The location of the distal end of the sensing wire 912 may be adjusted relative to the distal end of the tubular member (*e.g.*, catheter) 906. For example, the distal end of the sensing wire 912 may be moved so that a sensing element 912 is between 0 mm and 75 mm or between 0 mm and 100 mm from the distal end of the tubular member (*e.g.*, catheter) 906. It is noted that the sensing wire 912 may be used to sense a first set of pressures within the target vessel 900 while a fluid (*e.g.*, an infusate) comprising a therapeutic agent is being delivered through the distal opening of the lumen of the tubular member (*e.g.*, catheter) 906 as in the step illustrated by Fig. 22D. Therefore, the sensing wire 912 may, for example, be positioned at a location suitable for sensing a pressure within the target vessel 900 while the therapeutic agent is being delivered through the distal opening of the lumen of the tubular member (*e.g.*, catheter) 906. Then, also as shown in Fig. 22D, the lumen of the tubular member (*e.g.*, catheter) 906 may be flushed with contrast and/or saline 914. Flushing the lumen of the tubular member (*e.g.*, catheter) 906 with contrast and/or saline 914 may generate higher pressure within the vasculature distal to the microvalve vessel occluder 908 and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor 902. It is noted that the sensing wire 912 may also be used to sense a second set of pressures within the target vessel 900 while the contrast and/or saline 914 is being delivered through the distal opening of the lumen of the tubular member (*e.g.*, catheter) 906. Therefore, the sensing wire 912 may, for example, be positioned at a location that is also suitable for sensing a pressure within the target vessel 900 while the contrast and/or saline 914 is being delivered through the distal opening of the lumen of the tubular member (*e.g.*, catheter) 906.

[00209] Turning now to Figs. 23A through 23D, exemplary configurations for a treatment system in an exemplary method of delivering a therapeutic agent within a vasculature of a patient are shown. The treatment systems discussed above, in particular, treatment system 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel 1000 in fluid communication with,

for example, a solid tumor 1002 of an organ according to the method illustrated by Figs. 23A through 23D discussed herein. As shown in Fig. 23A, a microcatheter 1004 may be moved, in particular, advanced distally into the vasculature, until a distal end of the microcatheter 1004 reaches a first location. Then, as shown in Fig. 23B, a tubular member (*e.g.*, catheter) 1006 comprising a microvalve vessel occluder 1008 may be moved, in particular, advanced distally into the vasculature, over the microcatheter 1004 through a distal opening of a lumen of the tubular member (*e.g.*, catheter) 1006 until a distal end of the tubular member (*e.g.*, catheter) 1006 and/or the microvalve vessel occluder 1008 reaches a target occlusion location. The first location of the distal end of the microcatheter 1004 may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion location. The microcatheter 1004 may then be removed (*i.e.*, withdrawn) from the target vessel 1000 through the lumen of the tubular member (*e.g.*, catheter) 1006. Then, as shown in Fig. 23C, a fluid (*e.g.*, an infusate) comprising a therapeutic agent 1010 may be delivered through the distal opening of the lumen of the tubular member (*e.g.*, catheter) 1006 causing the microvalve vessel occluder 1008 to expand when vascular pressure distal to the microvalve vessel occluder 1008 exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder 1008. Furthermore, the microvalve vessel occluder 1008 may be configured to dynamically move with pressure change such that when the pressure distal to the microvalve vessel occluder 1008 exceeds and/or becomes greater than the pressure proximal to the microvalve vessel occluder 1008, the microvalve vessel occluder 1008 expands and/or fully expands to prevent reflux. Then, as shown in Fig. 23D, the lumen of the tubular member (*e.g.*, catheter) 1006 may be flushed with contrast and/or saline 1012. Flushing the lumen of the tubular member (*e.g.*, catheter) 1006 with contrast and/or saline 1012 may generate higher pressure within the vasculature distal to the microvalve vessel occluder 1008 and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor 1002.

[00210] Turning now to Figs. 24A through 24D, exemplary configurations for a treatment system in an exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient are shown. The treatment systems described above, in particular, treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel 1100 in fluid communication with, for example, a solid tumor 1102 of an organ

according to the method illustrated by Figs. 24A through 24D discussed herein. Figs. 24A-24C are substantially the same as Figs. 23A-23C described above, with like components being numbered with like reference numerals. As shown in Fig. 24A, a microcatheter 1104 may be moved until a distal end of the microcatheter 1104 reaches a first location. Then, as shown in Fig. 24B, a catheter 1106 comprising a microvalve vessel occluder 1108 may be moved over the microcatheter 1104 through a distal opening of a lumen of the catheter 1106 until a distal end of the catheter 1106 and/or the microvalve vessel occluder 1108 reaches a target occlusion location. The microcatheter 1104 may then be removed from the target vessel 1100 through the lumen of the tubular member (e.g., catheter) 1006. Then, as shown in Fig. 24C, therapeutic agent 1110 may be delivered through the distal opening of the lumen of the catheter 1106 causing the microvalve vessel occluder 1108 to expand when vascular pressure distal to the microvalve vessel occluder 1108 exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder 1108. Then, as shown in Fig. 24D, a distal end of a sensing wire 1112 may then be moved to a sensing location within the vasculature of the patient in the same manner as discussed above with respect to Fig. 22D. The location of the distal end of the sensing wire 1112 may be adjusted relative to the distal end of the catheter 1106. It is noted that the sensing wire 1112 may be used to sense a first set of pressures within the target vessel 1100 while a fluid (e.g., an infusate) comprising a therapeutic agent is being delivered through the distal opening of the lumen of the catheter 1106 as in the step illustrated by Fig. 24D. Therefore, the sensing wire 1112 may, for example, be positioned at a location suitable for sensing a pressure within the target vessel 1100 while the therapeutic agent is being delivered through the distal opening of the lumen of the catheter 1106. Then, also as shown in Fig. 24D, the lumen of the catheter 1106 may be flushed with contrast and/or saline 1114 in the same manner as discussed above with respect to Fig. 22D. It is noted that the sensing wire 1112 may also be used to sense a second set of pressures within the target vessel 1100 while the contrast and/or saline 1114 is being delivered through the distal opening of the lumen of the catheter 1106. Therefore, the sensing wire 1112 may, for example, be positioned at a location that is also suitable for sensing a pressure within the target vessel 1100 while the contrast and/or saline 1114 is being delivered through the distal opening of the lumen of the catheter 1106.

[00211] Turning now to Figs. 25A through 25D, exemplary configurations for a treatment system in an exemplary method of delivering a fluid (e.g., an infusate) comprising a therapeutic agent within a vasculature of a patient are shown. The treatment systems discussed above, in

particular, treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (e.g., an infusate) comprising a therapeutic agent into a target vessel 1200 in fluid communication with, for example, a solid tumor 1202 of an organ according to the method illustrated by Figs. 25A through 25D discussed herein. Figs. 25A-25B are substantially the same as Figs. 23A-23B described above, with like components being numbered with like reference numerals. As shown in Fig. 25A, a microcatheter 1204 may be moved until a distal end of the microcatheter 1204 reaches a first location. Then, as shown in Fig. 25B, a catheter 1206 comprising a microvalve vessel occluder 1208 may be moved over the microcatheter 1204 through a distal opening of a lumen of the catheter 1206 until a distal end of the catheter 1206 and/or the microvalve vessel occluder 1208 reaches a target occlusion location. The microcatheter 1204 may then be removed (*i.e.*, withdrawn) from the target vessel 1200 through the lumen of the catheter 1206.

[00212] Then, as shown in Fig. 25C, a distal end of a sensing wire 1212 may be moved to a sensing location within the vasculature of the patient and a fluid (e.g., an infusate) comprising a therapeutic agent 1210 may be delivered through the distal opening of the lumen of the catheter 1206 causing the microvalve vessel occluder 1208 to expand when vascular pressure distal to the microvalve vessel occluder 1208 exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder 1208. The location of the distal end of the sensing wire 1212 may be adjusted relative to the distal end of the catheter 1206 to sense a pressure within the target vessel 1200. For example, the distal end of the sensing wire 1212 may be moved so that a sensing element 1212 is between 0 mm and 75 mm, or between 0 mm and 100 mm from the distal end of the catheter 1206. It is noted that the sensing wire 1212 may be used to sense a first set of pressures within the target vessel 1200 while a fluid (e.g., an infusate) comprising a therapeutic agent is being delivered through the distal opening of the lumen of the catheter 1206 as in the step illustrated by Fig. 25C. Therefore, the sensing wire 1212 may, for example, be positioned at a location suitable for sensing a pressure within the target vessel 1200 while the therapeutic agent is being delivered through the distal opening of the lumen of the catheter 1206. Then, as shown in Fig. 25D, the lumen of the catheter 1206 may be flushed with contrast and/or saline 1214. It is noted that the sensing wire 1212 may also be used to sense a second set of pressures within the target vessel 1200 while the contrast and/or saline 1214 is being delivered through the distal opening of the lumen of the catheter 1206 as in the step illustrated by Fig. 25D. Therefore, the

sensing wire 1212 may, for example, be positioned at a location that is also suitable for sensing a pressure within the target vessel 1200 while the contrast and/or saline 1214 is being delivered through the distal opening of the lumen of the catheter 1206. Flushing the lumen of the catheter 1206 with contrast and/or saline 1214 may generate higher pressure within the vasculature distal to the microvalve vessel occluder 1208 and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor 1202.

[00213] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment system 600 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a guidewire may be moved, in particular, advanced distally into the vasculature, to a target infusion location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the guidewire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches the target infusion location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the tubular member (*e.g.*, catheter) and/or the microvalve vessel occluder reaches a target occlusion location. The target infusion location of the distal end of the microcatheter may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion location. The guidewire may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the microcatheter. A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the microcatheter causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. The method may further comprise removing (*i.e.*, withdrawing) the microcatheter from the target vessel through the lumen of the tubular member (*e.g.*, catheter) and flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline. Flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline may generate higher pressure within the vasculature distal to the microvalve vessel occluder and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor.

[00214] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment systems discussed above, in particular, treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a guidewire may be moved, in particular, advanced distally into the vasculature, to a target infusion location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the guidewire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches the target infusion location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the tubular member (*e.g.*, catheter) and/or the microvalve vessel occluder reaches a target occlusion location. The target infusion location of the distal end of the microcatheter may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion location. The guidewire may then be removed (*i.e.*, withdrawn) from the lumen of the microcatheter. A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the microcatheter causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. Then, the microcatheter may be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the tubular member (*e.g.*, catheter). A distal end of a sensing wire may then be moved to a sensing location within the vasculature of the patient. The location of the distal end of the sensing wire may be adjusted relative to the distal end of the tubular member (*e.g.*, catheter). For example, the distal end of the sensing wire may be moved so that a sensing element is between 0 mm and 75 mm or between 0 mm and 100 mm from the distal end of the tubular member (*e.g.*, catheter). It is noted that the sensing wire or sensing element(s) may be used to sense a first set of pressures within the target vessel while a fluid (*e.g.*, an infusate) comprising a therapeutic agent is being delivered to the target infusion location. Then, the lumen of the tubular member (*e.g.*, catheter) may be flushed with contrast and/or saline. Flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline may generate higher pressure within the vasculature distal to the microvalve vessel occluder and increase therapy

penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor. It is noted that the sensing wire may also be used to sense a second set of pressures within the target vessel while the contrast and/or saline is being delivered.

[00215] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment systems discussed above, in particular, treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a sensing wire may be moved to a sensing location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the sensing wire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches a target infusion location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the tubular member (*e.g.*, catheter) and/or the microvalve vessel occluder reaches a target occlusion location. The target infusion location of the distal end of the microcatheter may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion location. A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the microcatheter causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. It is noted that the sensing wire or sensing element(s) may be used to sense a first set of pressures within the target vessel while a fluid (*e.g.*, an infusate) comprising a therapeutic agent is being delivered to the target infusion location. The sensing wire may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the microcatheter. The method may further comprise removing (*i.e.*, withdrawing) the microcatheter from the target vessel through the lumen of the tubular member (*e.g.*, catheter) and flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline. Flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline may generate higher pressure within the vasculature distal to the microvalve vessel occluder and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor. Alternatively, the sensing wire is not removed from the

target vessel before flushing of the lumen of the tubular member (*e.g.*, catheter) and the sensing wire or sensing element(s) may also be used to sense a second set of pressures within the target vessel while the contrast and/or saline is being delivered.

[00216] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment systems discussed above, in particular, treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a sensing wire may be moved to a sensing location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the sensing wire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches a target infusion location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the tubular member (*e.g.*, catheter) and/or the microvalve vessel occluder reaches a target occlusion location. The target infusion location of the distal end of the microcatheter may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion location. A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the microcatheter causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. It is noted that the sensing wire or sensing element(s) may be used to sense a first set of pressures within the target vessel while a fluid (*e.g.*, an infusate) comprising a therapeutic agent is being delivered to the target infusion location. The sensing wire may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the microcatheter. Then, the microcatheter may be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the tubular member (*e.g.*, catheter). A distal end of a sensing wire may then be moved to a sensing location within the vasculature of the patient. The sensing location of the distal end of the sensing wire may be adjusted relative to the distal end of the tubular member (*e.g.*, catheter). For example, the distal end of the sensing wire may be moved so that a sensing element is between 0 mm and 75 mm or between 0 mm and 100 mm from the distal end of the tubular member (*e.g.*, catheter). Then, the

lumen of the tubular member (*e.g.*, catheter) may be flushed with contrast and/or saline. Flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline may generate higher pressure within the vasculature distal to the microvalve vessel occluder and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor. Alternatively, the sensing wire is not removed from the target vessel before flushing of the lumen of the tubular member (*e.g.*, catheter) and the sensing wire or sensing element(s) may also be used to sense a second set of pressures within the target vessel while the contrast and/or saline is being delivered.

[00217] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a guidewire may be moved, in particular, advanced distally into the vasculature, to a target infusion location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the guidewire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches the target infusion location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the tubular member (*e.g.*, catheter) and/or the microvalve vessel occluder reaches a target occlusion location. The target infusion location of the distal end of the microcatheter may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion location. The guidewire may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the microcatheter. A distal end of a sensing wire may then be moved to a sensing location within the vasculature of the patient. The sensing location of the distal end of the sensing wire may be adjusted relative to the distal end of the tubular member (*e.g.*, catheter). For example, the distal end of the sensing wire may be moved so that a sensing element is between 0 mm and 75 mm or between 0 mm and 100 mm from the distal end of the tubular member (*e.g.*, catheter). A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the microcatheter causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds

and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. It is noted that the sensing wire or sensing element(s) may be used to sense a first set of pressures within the target vessel while a fluid (*e.g.*, an infusate) comprising a therapeutic agent is being delivered to the target infusion location. The method may further comprise removing (*i.e.*, withdrawing) the microcatheter from the target vessel through the lumen of the tubular member (*e.g.*, catheter) and flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline. Flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline may generate higher pressure within the vasculature distal to the microvalve vessel occluder and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor. In one example, the microcatheter may be removed from the target vessel while the sensing wire remains in place. The sensing wire or sensing element(s) may also be used to sense a second set of pressures within the target vessel while the contrast and/or saline is being delivered.

[00218] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment system systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel communicating with, for example, a solid tumor of an organ. A distal end of a sensing wire may be moved to a sensing location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the sensing wire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches a target infusion location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the tubular member (*e.g.*, catheter) and/or the microvalve vessel occluder reaches a target occlusion location. The target infusion location of the distal end of the microcatheter may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion location. A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the microcatheter causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. The method may further comprise removing (*i.e.*,

withdrawing) the microcatheter from the target vessel through the lumen of the tubular member (*e.g.*, catheter) and flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline. Flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline may generate higher pressure within the vasculature distal to the microvalve vessel occluder and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor. In one example, the microcatheter may be removed from the target vessel while the sensing wire remains in place. The sensing wire or sensing element(s) may also be used to sense a second set of pressures within the target vessel while the contrast and/or saline is being delivered.

[00219] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a guidewire may be moved, in particular, advanced distally into the vasculature, to a first location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the guidewire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches a target infusion location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the tubular member (*e.g.*, catheter) or the microvalve vessel occluder reaches a target occlusion location. The first location of the distal end of the guidewire may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target infusion location of the distal end of the microcatheter. The target infusion location of the distal end of the microcatheter may be distal (*i.e.*, downstream in arteries and upstream in veins) to the target occlusion location. The guidewire and microcatheter may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the tubular member (*e.g.*, catheter). A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the tubular member (*e.g.*, catheter) causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. The method may further comprise flushing the lumen of the

tubular member (*e.g.*, catheter) with contrast and/or saline. Flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline may generate higher pressure within the vasculature distal to the microvalve vessel occluder and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor.

[00220] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a guidewire may be moved, in particular, advanced distally into the vasculature, to a target infusion location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the guidewire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches the target infusion location. The guidewire may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the microcatheter. A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the microcatheter.

[00221] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a guidewire may be moved, in particular, advanced distally into the vasculature, to a first location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the guidewire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches the first location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the tubular member (*e.g.*, catheter) and/or the microvalve vessel occluder reaches a target occlusion location. The first location of the distal end of the microcatheter may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion location. The guidewire may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the microcatheter.

The microcatheter may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the tubular member (*e.g.*, catheter). The guidewire and microcatheter may be removed simultaneously, the guidewire may first be removed then the microcatheter may be removed, and/or the microcatheter may first be removed then the guidewire may be removed. A distal end of a sensing wire may then be moved to a sensing location within the vasculature of the patient. The location of the distal end of the sensing wire may be adjusted relative to the distal end of the tubular member (*e.g.*, catheter). For example, the distal end of the sensing wire may be moved so that a sensing element is between 0 mm and 75 mm or between 0 mm and 100 mm from the distal end of the tubular member (*e.g.*, catheter). A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the tubular member (*e.g.*, catheter) causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. It is noted that the sensing wire or sensing element(s) may be used to sense pressures within the target vessel while a fluid (*e.g.*, an infusate) comprising a therapeutic agent is being delivered to the target infusion location.

[00222] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a guidewire may be moved, in particular, advanced distally into the vasculature, to a first location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the guidewire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches the first location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the tubular member (*e.g.*, catheter) or the microvalve vessel occluder reaches a target occlusion location. The first location of the distal end of the microcatheter may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion location. The guidewire may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the microcatheter. The microcatheter may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of

the tubular member (*e.g.*, catheter). The guidewire and microcatheter may be removed simultaneously, the guidewire may first be removed then the microcatheter may be removed, and/or the microcatheter may first be removed then the guidewire may be removed. A distal end of a sensing wire may then be moved to a sensing location within the vasculature of the patient. The sensing location of the distal end of the sensing wire may be adjusted relative to the distal end of the tubular member (*e.g.*, catheter). For example, the distal end of the sensing wire may be moved so that a sensing element is between 0 mm and 75 mm or between 0 mm and 100 mm from the distal end of the tubular member (*e.g.*, catheter). A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the tubular member (*e.g.*, catheter) causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. It is noted that the sensing wire or sensing element(s) may be used to sense a first set of pressures within the target vessel while a fluid (*e.g.*, an infusate) comprising a therapeutic agent is being delivered to the target infusion location. Then, the lumen of the tubular member (*e.g.*, catheter) may be flushed with contrast and/or saline. Flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline may generate higher pressure within the vasculature distal to the microvalve vessel occluder and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor. It is noted that the sensing wire may also be used to sense a second set of pressures within the target vessel while the contrast and/or saline is being delivered.

[00223] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a guidewire may be moved, in particular, advanced distally into the vasculature, to a first location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the guidewire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches a target infusion location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the

tubular member (*e.g.*, catheter) and/or the microvalve vessel occluder reaches a target occlusion location. The guidewire may then be removed (*i.e.*, withdrawn) from the blood vessel through the lumen of the microcatheter. A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the microcatheter causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. The distal end of the microcatheter may then be moved to a second target infusion location. The guidewire may be used to assist in the movement of the distal end of the microcatheter to the second target infusion location. A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the microcatheter while the distal end of the microcatheter is located at the second target infusion location. The distal end of the microcatheter may then be moved to one or more other target infusion locations with or without the use of the guidewire and a fluid (*e.g.*, an infusate) comprising the therapeutic agent may then be delivered at each target infusion location. After each and every infusion, the lumen of tubular member (*e.g.*, catheter) may be flushed with contrast and/or saline. Alternatively, after one or more infusions the lumen of tubular member (*e.g.*, catheter) may be flushed with contrast and/or saline. Alternatively, after the last infusion the lumen of tubular member (*e.g.*, catheter) may be flushed with contrast and/or saline. In some examples, the sensing wire may be used to measure a characteristic (*e.g.*, fluid pressure, vascular pressure, infusion pressure, flow rate, and/or infusion volume) of the first infusion and/or second infusion.

[00224] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, the treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communication with, for example, a solid tumor of an organ. A distal end of a first guidewire may be moved, in particular, advanced distally into the vasculature, to a first location within the vasculature of the patient. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the guidewire through a distal opening of a lumen of the tubular member (*e.g.*, catheter) until a distal end of the tubular member (*e.g.*, catheter) and/or the microvalve vessel occluder reaches a target occlusion location. The first guidewire may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the tubular member (*e.g.*,

catheter). A distal end of a second guidewire may be moved, in particular, advanced distally through a lumen of the tubular member (*e.g.*, catheter) into the vasculature, to a second location within the vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the second guidewire and through the lumen of the tubular member (*e.g.*, catheter) until a distal end of the microcatheter reaches a target infusion location. A fluid (*e.g.*, an infusate) comprising a therapeutic agent may then be delivered through the distal opening of the lumen of the microcatheter causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder.

[00225] In another exemplary method of delivering a fluid (*e.g.*, an infusate) comprising a therapeutic agent within a vasculature of a patient, a treatment system discussed above, in particular, treatment systems 10, 600, 700, 2600, 2700, 2800, 2900, 3000, 3100, and 3200 described above can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent can be used to inject a fluid (*e.g.*, an infusate) comprising a therapeutic agent into a target vessel in fluid communications with, for example, a solid tumor of an organ. A distal end of a guidewire may be moved to a location within the target vasculature of the patient. A microcatheter may then be moved, in particular, advanced distally into the vasculature, over the guidewire through a distal opening of a lumen of the microcatheter until a distal end of the microcatheter reaches a first infusion location. A tubular member (*e.g.*, catheter) comprising a microvalve vessel occluder may then be moved, in particular, advanced distally into the vasculature, over the microcatheter through a distal opening of a lumen of the catheter, until a distal end of the catheter and/or the microvalve vessel occluder reaches a target occlusion location. The first infusion location of the distal end of the microcatheter may be coincident to, or distal (*i.e.*, downstream in arteries and upstream in veins) of the target occlusion location of the distal end of the tubular member (*e.g.*, catheter). The first infusion location may be in vasculature distal to the target occlusion location in a vessel that does not directly feed target tissue (non-target vessel). The microcatheter may be used to deliver an embolizing agent (*e.g.*, a coil embolization agent, a gel embolizing agent, a glue embolizing agent, etc.) to a non-targeted vessel (for example, a blood vessel that is not in fluid communications with the tumor) to prevent blood flow to the non-targeted vessel. The microcatheter may then be removed (*i.e.*, withdrawn) from the target vessel through the lumen of the tubular member (*e.g.*, catheter). A distal end of a sensing wire may then be advanced through the catheter and moved to

a sensing location within the vasculature of the patient. The sensing location of the distal end of the sensing wire may be adjusted relative to the distal end of the tubular member (*e.g.*, catheter). For example, the distal end of the sensing wire may be moved so that a sensing element is between 0 mm and 75 mm or between 0 mm and 100 mm from the distal end of the tubular member (*e.g.*, catheter). A fluid (*e.g.*, an infusate comprising a therapeutic agent) may then be delivered to the target infusion location in the target vessel through the distal opening of the lumen of the tubular member (*e.g.*, catheter) causing the microvalve vessel occluder to expand when vascular pressure distal to the microvalve vessel occluder exceeds and/or becomes greater than the vascular pressure proximal to the microvalve vessel occluder. The fluid is prevented from flowing to the non-targeted vessel embolized by the microcatheter. The sensing wire may measure the delivery properties of the fluid (*e.g.*, an infusate) comprising therapeutic agent (*e.g.*, pressure, flow rate, volume of the delivery of the fluid). It is noted that the sensing wire or sensing element(s) may be used to sense a first set of pressures within the target vessel while a fluid (*e.g.*, an infusate) comprising a therapeutic agent is being delivered to the target infusion location. The method may further comprise flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline. Flushing the lumen of the tubular member (*e.g.*, catheter) with contrast and/or saline may generate higher pressure within the vasculature distal to the microvalve vessel occluder and increase therapy penetration (*i.e.*, penetration of the fluid (*e.g.*, infusate) or therapeutic agent) into the solid tumor. It is noted that the sensing wire may also be used to sense a second set of pressures within the target vessel while the contrast and/or saline is being delivered.

[00226] The treatment systems described above may be used with the following exemplary methods for delivering a fluid (*e.g.*, an infusate) into a target vessel in fluid communication with, for example, a solid tumor of an organ.

[00227] An exemplary method 3500 of delivering a fluid (*e.g.*, an infusate) comprising one or more therapeutic agents is shown in Fig. 35. In an exemplary method a treatment system may, for example, deliver a therapeutic agent to a tumor in fluid communication with a vascular system of an organ of a patient. An exemplary method 3600 of delivering one or more therapeutic agents is shown in Fig. 36. The method of Fig. 36 is substantially similar to the method shown in Fig. 35, with step 3602 to 3614 corresponding to steps 3502 to 3514 and step 3516 corresponding to step 3518. An exemplary method 3700 of delivering one or more therapeutic agents is shown in Fig. 37. The method of Fig. 37 is substantially similar to the method shown in Fig. 35, with step 3702

to 3704 corresponding to steps 3502 to 3504, steps 3706 to 3708 corresponding to steps 3508 to 3510 and steps 3710 to 3712 corresponding to step 3512 to 3514, and step 3714 corresponding to step 3518.

[00228] An exemplary method 3800 of delivering one or more therapeutic agents is shown in Figure 38. In an exemplary method a treatment system may, for example, deliver a therapeutic agent to a tumor in fluid communication with a vascular system of an organ of a patient. An exemplary method 3900 of delivering one or more therapeutic agents is shown in Fig. 39. The method of Fig. 39 is substantially similar to the method shown in Fig. 38, with step 3902 to 3918 corresponding to steps 3802 to 3818, steps 3920 to 3922 corresponding to steps 3822 to 3824.

An exemplary method 4000 of delivering one or more therapeutic agents is shown in Figure 40. The method of Fig. 40 is substantially similar to the method shown in Fig. 38, with step 4002 to 4004 corresponding to steps 3802 to 3804, step 4006 corresponding to step 3808, step 4010 to 4014 corresponding to steps 3814 to 3818, and step 4016 to 4018 corresponding to steps 3822 to 3824.

[00229] Additionally, it is contemplated that that the treatment systems and method described herein may be used for delivery of a fluid (*e.g.*, an infusate) comprising a therapeutic agent to an arterial system of the liver.

[00230] The occluder of the treatment system may be positioned in a target occlusion location in the celiac artery, and the infusate may be delivered at a target infusion position at least one bifurcation distally past the celiac artery and in the common or proper hepatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the celiac artery, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the celiac artery and in the right, left, or medial hepatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the celiac artery, and the infusate may be delivered at a target infusion position at least three bifurcations distally past the celiac artery and in the segmental arterial branches of the right, left, or medial hepatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the celiac artery, and the infusate may be delivered at a target infusion position at least four bifurcations distally past the celiac artery and in the sub-segmental arterial branches of the right, left, or medial hepatic artery.

[00231] The occluder of the treatment system may be positioned in a target occlusion location

in the common hepatic artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the common hepatic artery and in the right, left, or medial hepatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the common hepatic artery, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the common hepatic artery and in the segmental arterial branches of the right, left, or medial hepatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the common hepatic artery, and the infusate may be delivered at a target infusion position at least three bifurcations distally past the common hepatic artery and in the sub-segmental arterial branches of the right, left, or medial hepatic artery.

[00232] The occluder of the treatment system may be positioned in a target occlusion location in the proper hepatic artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the proper hepatic artery and in the proper hepatic artery and into the right, left, or medial hepatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the proper hepatic artery, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the proper hepatic artery and in the segmental arterial branches of the right, left, or medial hepatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the proper hepatic artery, and the infusate may be delivered at a target infusion position at least three bifurcations distally past the proper hepatic artery and in the sub-segmental arterial branches of the right, left, or medial hepatic artery.

[00233] The occluder of the treatment system may be positioned in a target occlusion location in the right hepatic artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the right hepatic artery and in the posterior segmental artery or anterior segmental artery. The occluder of the treatment system may be positioned in a target occlusion location in the right hepatic artery, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the right hepatic artery and in the right hepatic artery and in the into segment 1, 5, 6, 7, or 8 arterial branches of the right hepatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the right hepatic artery, and the infusate may be delivered at a target infusion position at least three bifurcations distally past the right hepatic artery and in the right hepatic artery and in the sub-segmental arterial branches of segment 1, 5, 6, 7, or 8 arterial branches of the right hepatic artery.

[00234] The occluder of the treatment system may be positioned in a target occlusion location in the left hepatic artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the left hepatic artery and in the posterior segmental artery or anterior segmental artery. The occluder of the treatment system may be positioned in a target occlusion location in the left hepatic artery, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the left hepatic artery and in the left hepatic artery and in the into segment 1, 5, 6, 7, or 8 arterial branches of the left hepatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the left hepatic artery, and the infusate may be delivered at a target infusion position at least three bifurcations distally past the left hepatic artery and in the left hepatic artery and in the sub-segmental arterial branches of segment 1, 5, 6, 7, or 8 arterial branches of the left hepatic artery.

[00235] Additionally, it is contemplated that that the treatment systems and method described herein may be used for delivery of a fluid (*e.g.*, an infusate) comprising a therapeutic agent to an arterial system of the prostate.

[00236] The occluder of the treatment system may be positioned in a target occlusion location in the internal iliac artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the internal iliac artery and in the anterior or posterior iliac trunk. The occluder of the treatment system may be positioned in a target occlusion location in the internal iliac artery, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the internal iliac artery and in the ombilical artery, obturator artery, deferential artery, superior vesical artery, middle rectal artery, internal pudendal artery, inferior gluteal artery, superior gluteal artery, lateral sacral artery, or ilio-lumbar artery.

[00237] The occluder of the treatment system may be positioned in a target occlusion location in the anterior iliac artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the anterior iliac artery and in the ombilical artery, obturator artery, deferential artery, superior vesical artery, middle rectal artery, internal pudendal artery, or inferior gluteal artery.

[00238] The occluder of the treatment system may be positioned in a target occlusion location in the posterior iliac artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the posterior iliac artery and in the superior gluteal artery, lateral sacral artery, or ilio-lumbar artery.

[00239] Additionally, it is contemplated that that the treatment systems and method described herein may be used for delivery of a fluid (*e.g.*, an infusate) comprising a therapeutic agent to an arterial system of the uterus.

[00240] The occluder of the treatment system may be positioned in a target occlusion location in the internal iliac artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the internal iliac artery and in the uterine artery. The occluder of the treatment system may be positioned in a target occlusion location in the internal iliac artery, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the internal iliac artery and in the branches of the uterine artery.

[00241] The occluder of the treatment system may be positioned in a target occlusion location in the uterine artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the uterine artery and in the branches of the uterine artery.

[00242] Additionally, it is contemplated that that the treatment systems and method described herein may be used for delivery of a fluid (*e.g.*, an infusate) comprising a therapeutic agent to an arterial system of the thyroid.

[00243] The occluder of the treatment system may be positioned in a target occlusion location in the thyrocervical trunk, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the thyrocervical trunk and in the inferior thyroid artery. The occluder of the treatment system may be positioned in a target occlusion location in the thyrocervical trunk, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the thyrocervical trunk and in a branch of the inferior thyroid artery.

[00244] The occluder of the treatment system may be positioned in a target occlusion location in the inferior thyroid artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past inferior thyroid artery and in a branch of the inferior thyroid artery.

[00245] Additionally, it is contemplated that that the treatment systems and method described herein may be used for delivery of a fluid (*e.g.*, an infusate) comprising a therapeutic agent to an arterial system of the pancreas.

[00246] The occluder of the treatment system may be positioned in a target occlusion location in the coceliac artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the coceliac artery and in the splenic artery or gastroduodenal artery. The occluder of the treatment system may be positioned in a target occlusion location in the coceliac

artery, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the celiac artery and in the posterior pancreatic artery, transverse pancreatic artery, large pancreatic artery, or short pancreatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the celiac artery, and the infusate may be delivered at a target infusion position at least three bifurcations distally past the celiac artery and in the branches of the posterior pancreatic artery, transverse pancreatic artery, large pancreatic artery, or short pancreatic artery.

[00247] The occluder of the treatment system may be positioned in a target occlusion location in the splenic artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the splenic artery and in the posterior pancreatic artery, transverse pancreatic artery, large pancreatic artery, or short pancreatic artery. The occluder of the treatment system may be positioned in a target occlusion location in the splenic artery, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the splenic artery and in the branches of the posterior pancreatic artery, transverse pancreatic artery, large pancreatic artery, or short pancreatic artery.

[00248] The occluder of the treatment system may be positioned in a target occlusion location in the gastroduodenal artery, and the infusate may be delivered at a target infusion position at least one bifurcations distally past the gastroduodenal artery and in the anterior or posterior arterial arcade of the pancreas. The occluder of the treatment system may be positioned in a target occlusion location in the gastroduodenal artery, and the infusate may be delivered at a target infusion position at least two bifurcations distally past the gastroduodenal artery and in the branches of the anterior or posterior arterial arcade of the pancreas.

[00249] The one or more target infusion locations may be one or more semi-selective locations, one or more selective locations, and/or one or more super selective locations. A semi-selective infusion location is further upstream, proximal, and/or fewer bifurcations from the aorta than a selective or super selective location. For example, a semi-selective infusion location may supply blood to a part and/or a portion of a lobe of a liver, the lobe of the liver comprising multiple segments. A selective location is further upstream, proximal, and/or fewer bifurcations from the aorta than a super selective location. A selective location is further distal (*i.e.*, downstream in arteries) and/or more bifurcations from the aorta than a semi-selective location. For example, a selective location may supply blood to a segment within a lobe of a liver. A super selective location

is further downstream, distal, and/or more bifurcations from the aorta than a semi-selective or selective location. For example, a super selective location may supply blood to a part and/or a portion of a segment within a lobe of a liver. The plurality of target infusion locations may be located less than one centimeter from one another, one centimeter from one another, and/or more than one centimeter from one another. The one or more target infusion locations may be located less than one centimeter from the target occlusion location, one centimeter from the target occlusion location, and/or more than one centimeter from the target occlusion location.

[00250] Although the examples above describes moving each component in sequence, it is contemplated that the sensing wire, guidewire, microcatheter, and/or catheter may be moved simultaneously in the vasculature of the patient. For example, the guidewire and microcatheter may be moved simultaneously in the vasculature of the patient. In another example, the sensing wire and catheter may be moved simultaneously in the vasculature of the patient. In a further example, the sensing wire and microcatheter may be moved simultaneously in the vasculature of the patient. In a further example, the sensing wire and catheter may be moved simultaneously in the vasculature of the patient. In a further example, the microcatheter and catheter may be moved simultaneously in the vasculature of the patient.

[00251] The sensing wire, guidewire, microcatheter, and/or catheter may further comprise one or more radiopaque marker bands. The movement of the sensing wire, guidewire, microcatheter, and/or catheter to one or more locations may be visualized using radiographic imaging of the one or more radiopaque marker bands of the sensing wire, guidewire, microcatheter, and/or catheter. For example, while the distal end of the guidewire is moved within the vasculature of the patient, the location of the distal end of the guidewire may be visualized using radiographic imaging. Then, if needed to reach the first location, the target infusion location, and/or the target occlusion location, the distal end of the guidewire may be moved again within the vasculature based on the visualization provided by the radiographic images. This may be repeated as needed until the desired location is reached. Similar steps may be performed for the sensing wire, microcatheter, and/or catheter.

[00252] The one or more injections, deliveries, infusions, flushings, and/or introductions of a fluid (e.g., an infusate) comprising a therapeutic agent, contrast agent, saline, drug, and/or other material described may be stopped, paused, ceased, and/or terminated when reflux into undesired and/or nontarget vessels occurs. The one or more injections, deliveries, infusions, flushings, and/or

introductions of a fluid (e.g., an infusate) comprising a therapeutic agent, contrast agent, saline, drug, and/or other material described may be stopped, paused, ceased, and/or terminated when a desired volume, weight, and/or amount of a fluid (e.g., an infusate) comprising a therapeutic agent, contrast agent, saline, drug, and/or other material has been injected, delivered, infused, flushed, and/or introduced. The one or more injections, deliveries, infusions, flushings, and/or introductions of a fluid (e.g., an infusate) comprising a therapeutic agent, contrast agent, saline, drug, and/or other material described may be stopped, paused, ceased, and/or terminated when a target vascular pressure has been reached and/or a plurality of target vascular pressures have been reached.

EXAMPLE

Example I:

[00253] In an example of delivery using the exemplary treatment system 2600 of Fig. 26, data was collected from an Oncopig model of hepatic cancer. The study tested the hypothesis that Pressure Enabled Drug Delivery (PEDD) with an exemplary treatment system would improve the delivery of surrogate therapeutic glass microspheres (GM) via hepatic artery infusion (HAI) to liver tumors when compared to a conventional endhole microcatheter.

[00254] Comparisons were made in selective infusion of GM into hepatic vessels leading to a tumor using either a conventional endhole microcatheter alone, or a microcatheter and an exemplary treatment system. A transgenic orthotopic liver tumor oncopig model was selected due to similarities in vascular size and hepatic anatomy with humans.

[00255] The study was conducted in male and female transgenic pigs (oncopigs) 25-45kg in weight. Hepatic tumors were induced according to the methodology described by Nurili F, Monette S, Michel AO, Bendet A, Basturk O, Askan G, et al. Transarterial Embolization of Liver Cancer in a Transgenic Pig Model. J Vase Interv Radiol 2021;32:510-517.e3, which is incorporated by reference herein in its entirety. In brief, the Oncopig is a transgenic porcine model that carries both KRASG12D and TP53R1 67H mutant oncogenes that are inducible by Cre recombinase. Liver biopsies were transformed after exposure to adenoviral vectors encoding Cre recombinase (AdCre) to induce oncogene expression and injected back into the liver at 4 locations to induce tumor formation. Induced tumors were allowed to grow for 8-10 days (1-3 cm in diameter) prior to treatment.

[00256] A fluorescently labeled silica glass microsphere (GM) was produced to simulate a Y90-like therapeutic infusion. Amine modified silica glass spheres (20µm mean diameter, 2.2g/cm²) were acquired from ERUI Biotech CO. Ltd, Shanghai (catalog number EPRUI-Si-20-NH₂ 2-003-20). A mass of 0.3096 grams of spheres were labeled using a 0.5 mg IRDye 800CW NHS Ester labeling kit (Li-Cor, Inc. Lincoln, NE, PIN 929-70020). Spheres were suspended in 10ml of pH 8.5 phosphate buffer solution (Cepharm Life Sciences, Inc. Fulton, MD). The IRDye was then dissolved in 500µl of ultrapure water and added to the sphere suspension. Labeling occurred in a light-shielded environment for 2 hours with the spheres undergoing gentle agitation. Labeled spheres were separated from the solution using a filter and washed three times in pH 7.4 phosphate buffered saline (Cepharm Life Sciences, Inc. Fulton, MD) prior to use.

[00257] The Seldinger technique was used to gain access through the femoral artery. A 6F introducer sheath (Pinnacle, Terumo Medical Corporation, Somerset, NJ) was secured at the site. A 5F guiding catheter was used to perform angiography to identify hepatic arterial anatomy and the vessels feeding the lesions. Tumors were hypovascular as assessed by angiography. Animals were randomly assigned and the infusion device, an exemplary treatment system comprising a microvalve vessel occluder such as a catheter with a dynamic occluder (commercially available as TriNav®) and a conventional endhole microcatheter were respectively alternated between.

[00258] A first tubular element of the exemplary treatment system was positioned in a 2.0-3.5mm in diameter vessel in fluid communication and feeding into 1 to 2 liver lobes, also referred to as a lobar position. A second tubular element of the exemplary treatment system comprising a microcatheter was then tracked to a distal selective position within vessel networks. This was typically a second or third order vessels 1.5-2.5mm in diameter in fluid communication with and feeding into 1/4 to 1/2 of a targeted lobe. Equivalent selective positions were used for both the conventional endhole microcatheter delivery and for the exemplary treatment system. Infusions were conducted when no signs of vasospasm and robust antegrade flow were present as assessed by a board-certified interventional radiologist with fluoroscopy prior to infusion.

[00259] A TheraSphere™ Administration Set (Biocompatibles UK Ltd.) was used to infuse a 6 GBq equivalent dose (2,400,000 spheres, 0.022117 grams) of GM according to an exemplary methodology described in the IFU. A total of 30ml of saline solution was infused during the procedure. Two sets of infusions for the exemplary treatment system were tested. The first group received only an infusion of a therapeutic agent before removal of the exemplary treatment system

(Low Pressure). The second group received a high pressure infusion of an infusate comprising contrast after the removal of the second tubular element comprising a microcatheter from the exemplary treatment system in order to generate elevated pressure within the distal vasculature (High Pressure). The duration of this infusion was 3-4 seconds. Angiography was performed following the infusion to ensure the position of the device had not changed during the infusion. Animals were euthanized 15 minutes after completion of the infusion.

[00260] Immediately after euthanasia, the liver was removed. The liver lobes were separated and nearIR imaging with a Pearl Trilogy Imaging System (Li-Cor, Inc. Lincoln, NE) was performed to identify patterns of therapeutic uptake. Each lobe was then cut into serial 1cm thick cross sections and imaged (85µm resolution, 700 nm, 800 nm, and white light channels) on both cut tissue faces using the Pearl system. The full liver volume was analyzed to determine the location of tumors and the presence of labeled microspheres within the tissue.

[00261] The slice of tissue containing a full thickness central (maximum diameter) section of the target tumor was identified. The 800 nm channel, corresponding to fluorescence from GM, was identified and processed through a custom ImageJ program to produce images readable by Visiopharm software (Visiopharm Co. Hoersholm, Denmark). Matching 18MP color images were taken of the slice and were also processed using the ImageJ conversion program. Visiopharm software was then utilized to overlay the color and nearIR images and the Visiopharm Deep Learning algorithm was used to identify normal liver tissue and tumor tissue. The tumor border was identified and 1mm concentric zones extending into and away from the tumor were delineated for data processing of surface area and nearIR signal intensity. Minitab Software (Minitab LLC, Chicago, IL) was employed to conduct one tailed paired t-tests (consistent with the hypothesis of increased delivery) between regions of interest in the conventional endhole delivery and delivery with the exemplary treatment system. In cases where multiple tumors were dosed during infusion, the tumor with the highest fluorescent signal was selected for analysis.

[00262] A total of 8 tumors were treated using only a conventional endhole microcatheter, 7 tumors were treated using the exemplary treatment system without a high pressure infusion, and 9 tumors were treated with the exemplary treatment system with a high pressure infusion.

[00263] Referring to Figure 41, infusion using an exemplary treatment system deposited high concentrations of therapeutic in and around the tumor. With the delivery of the therapeutic being more concentrated in the tumor and peritumor regions. Figure 41 shows the relative concentrations

of a therapeutic agent in tumor and peritumor regions. The left image of Figure 41 shows the concentration of a therapeutic agent after infusion with an exemplary treatment system using the above-described “High Pressure” method. The center image of Figure 41 shows the concentration of a therapeutic agent after infusion with an exemplary treatment system using the above-described “Low Pressure” method. The right image of Figure 41 shows the concentration of a therapeutic agent after infusion with a conventional endhole microcatheter.

[00264] Referring to Figure 42, a summary of the anatomical and methodological characteristics of the above-provided example is shown. The tumor diameter was similar for all infusions and 2.01 mm on average. The occluder of the exemplary treatment system was located in a proximal vessel whereas the secondary tubular element was located in a distal vessel. The proximal vessels were larger in diameter and were in fluid communication with a greater volume of tissue than the distal vessels. As shown in Figure 42, the second tubular element was displaced 35.04 ± 18.14 mm from the occluder. The occluder decreased average distal vascular pressure by $45.66 \pm 13.61\%$.

[00265] Referring to Figure 43, relative GM signal intensities are compared between concentric zones from -10 mm inward from the outer surface of the tumor to 30 mm outward from the outer surface of the tumor. Statistically significant increases in GM signal intensity were observed between the exemplary treatment system using the above-described “High Pressure” method and the exemplary treatment system using the above-described “High Pressure” method when compared to the conventional endhole microcatheter for each concentric zone from -10 mm inward from the outer surface of the tumor to 10 mm outward from the outer surface of the tumor ($p \leq 0.05$). No statistically significant difference was observed in concentric zones greater than 30 mm outward from the outer surface of the tumor. Use of the above-described “High Pressure” infusion through the exemplary treatment system resulted in a shift in distribution of the particles inward from the outer surface of the tumor relative to methods of therapy delivery without the use of the “High Pressure” infusion method.

[00266] Referring to Figure 44, statistically significant increases in total amount of therapy delivered to the tumor was observed for the exemplary treatment system relative to the conventional endhole microcatheter. Infusion with the exemplary treatment system alone increased the amount of therapy in the tumor by 62% relative to the conventional endhole microcatheter alone. The use of the above-described “High Pressure” method of infusion through

the exemplary treatment system further increased the amount of therapy delivery to the tumor. That is, the exemplary treatment system using the above-described “High Pressure” method of infusion increased therapy delivery to the tumor by 85% relative to the conventional endhole microcatheter alone.

[00267] The improved delivery with the above-described “High Pressure” method using the partially occlusive system is likely due to a combination of mechanisms. The occluder of the exemplary treatment system comprises a partial vessel occluder which blood pressure distal to an occlusion location by $46\% \pm 14\%$ relative to the initial pressure within the vessel. In response to this pressure drop, the body attempts to maintain a consistent pressure in the vessel in order to maintain adequate blood flow to distal tissues and achieve internal homeostasis. A drop in vascular pressure causes healthy vessels to constrict in an attempt to increase pressure and return to homeostasis.

[00268] In distinction, blood vessels in cancerous tissues are believed to lack the ordered smooth muscle architecture of normal vascular tissues. As such, it is believed that they are unable to adapt to changes in blood pressure or external stimulus. On the periphery of a large solid tumor, the aberrant physiology is believed to result in a zone of hypervascularization with large dilated arterial vessels. Blood pressure and resistance in such vessels is often lower than in surrounding tissue. If a decrease in blood pressure is experienced, normal healthy tissues is believed to undergo constriction, while the diseased tissue vessels is believed to remain open, low resistance vasculature.

[00269] Liver tissue also serves a blood reservoir function within the body, with 20-30% of the liver volume being blood. 50-60% of this volume can be expelled from the tissue due to both passive and active autoregulatory response. The normal hepatic venous bed actively constricts in response to $\alpha 2$ -adrenergic and angiotensin agonists released in response to blood pressure decrease. The vasculature is also elastic, leading to a passive capacitive volume. When pressure is reduced, the elastic vasculature relaxes, expelling blood and reducing in volume.

[00270] A localized decrease in pressure is therefore believed to trigger an increase in fluid resistance in the normal venous system as an active constrictive response is induced and a passive reduction in vessel volume due to the relaxation of elastic vessel walls. Normal liver volume is believed to be reduced and believed to become further resistant to flow. This in turn is believed to reduce compressive stresses on abnormal tumor tissue due to the reduction in volume of

surrounding normal tissues, potentially reducing resistance in tumor vasculature. The difference in vascular resistance in abnormal and normal tissues is believed to be further amplified, leading to increased flow to abnormal tissue. One or more therapeutic agents carried in this altered flow condition is believed to preferentially deposit in abnormal or cancerous tissue.

[00271] There have been described and illustrated herein examples of systems and methods for therapeutic delivery, and exemplary pressure-enabled therapeutic delivery. While particular embodiments of the treatment system and methods have been described, it is not intended that the invention be limited thereto, as it is intended that the invention be as broad in scope as the art will allow and that the specification be read likewise. Thus, while the systems and methods are primarily adapted for therapeutic treatment of humans, it has been demonstrated on porcine tissues and organs, and can be used for the treatment of mammals, in general. Both humans and animals shall be considered 'patients' for purpose of this disclosure. Furthermore, the steps of the exemplary methods of delivering a therapeutic agent within a vasculature may be performed in an alternative order, alternative orders, repeated, repeated in part, reversed, reversed in part, cycled, and/or cycled in part from the description provided above. Also, the therapy delivered herein can be a single therapeutic agent, or a combination of therapeutic agents. It will therefore be appreciated by those skilled in the art that yet other modifications could be made to the provided invention without deviating from its scope as claimed.

CLAIMS

What is Claimed is:

1. A treatment system for therapeutic delivery in a vessel of a patient, comprising:
 - a) a catheter having a proximal end and a distal end with a distal tip, an exterior, an infusion lumen defined from the proximal end and extending to the distal tip and opening at a distal orifice passing through the distal tip; and
 - b) a microvalve vessel occluder longitudinally displaceable over the exterior of the microcatheter.
2. The treatment system of claim 1, wherein the microvalve vessel occluder has a proximal side and distal side, and the microvalve vessel occluder is dynamic such that the microvalve vessel occluder automatically changes configuration based on the relative fluid pressure on the proximal and distal sides of the microvalve vessel occluder.
3. The treatment system of claim 2, wherein the microvalve vessel occluder includes a polymer coated braid of filaments provided on a tubular construct.
4. The treatment system of claim 1, wherein both the catheter and the microvalve vessel occluder include radiopaque markers to reference the location of the microvalve vessel occluder relative to the catheter.
5. The treatment system of claim 1, wherein the catheter includes a stop element to limit longitudinal displacement of the microvalve vessel occluder over the catheter.
6. The treatment system of any one of claims 1-5, further comprising:
 - an occluder pusher coupled to the microvalve vessel occluder and operable to longitudinally displace the microvalve vessel occluder over the exterior of the microcatheter.
7. The treatment system of claim 6, wherein the occluder pusher is a wire.

8. The treatment system of claim 7, wherein the tubular construct includes an eyelet and the wire is coupled to the eyelet.

9. The treatment system of claim 2, wherein at least one of the exterior of the catheter and an interior portion of the microvalve vessel occluder includes at least one rail, and the other of the catheter and the microvalve vessel occluder include at least one mating structure for the at least one rail, and the catheter and the microvalve vessel occluder can be displaced relative to each other on the at least one rail and that at least one mating structure.

10. The treatment system of claim 6, wherein the occluder pusher is a sheath extendable over the exterior of the microcatheter.

11. The treatment system of claim 6, wherein the microvalve vessel occluder is adapted to be advanced from the proximal end of the microcatheter to the distal end of the microcatheter in a reduced diameter, non-deployed configuration.

12. The treatment system of claim 11, wherein the occluder pusher is advanced to deploy the microvalve vessel occluder from a reduced diameter, non-deployed configuration to an expanded diameter, deployed configuration.

13. The treatment system of claim 12, wherein the microvalve vessel occluder includes a proximal end and a distal end, the microcatheter includes a distal stop to limit travel of the microvalve vessel occluder, and the occluder pusher is adapted to apply a compressive force between the proximal end of the microvalve vessel occluder and the distal stop.

14. A method of administering a fluid comprising a therapeutic agent into a blood vessel of an organ comprising:

a) advancing a distal tip at a distal end of a catheter into the blood vessel to a target infusion location, the catheter extending from a proximal end to the distal end, the catheter

comprises an external surface and a lumen extending from the proximal end to the distal end and opens at a distal orifice passing through the distal tip;

b) advancing a microvalve vessel occluder over the external surface of the catheter to a target occlusion location, wherein the microvalve vessel occluder is longitudinally displaceable over the catheter; and

c) infusing the fluid comprising the therapeutic agent through the lumen and out of the distal orifice of the catheter and into the blood vessel.

15. The method of claim 14, wherein the blood vessel is in fluid communication with a solid tumor.

16. The method of claim 14, further comprising:
advancing a guidewire into the blood vessel to the target infusion location, before step a), wherein the catheter is advanced into the blood vessel over the guidewire.

17. The method of claim 16, further comprising:
removing the guidewire before step c).

18. The method of claim 14, further comprising:
confirming the target occlusion location relative to the distal end of the catheter using radiographic imaging before step c).

19. The method of claim 14, wherein the blood vessel has branches distal of the target occlusion location of the microvalve vessel occluder.

20. The method of claim 19, wherein the target occlusion location is longitudinally displaced from the distal orifice such that the branches of the blood vessel are located between the distal orifice and the target occlusion location of the microvalve vessel occluder.

21. The method of claim 20, wherein the longitudinal displacement is about 5 mm to about 60 mm.

22. The method of claim 14, wherein the microvalve vessel occluder is advanced with a wire.
23. The method of claim 14, wherein the microvalve vessel occluder is advanced with an oversheath.
24. The method of claim 14, further comprising:
expanding the diameter of the microvalve vessel occluder before infusing.
25. The method of claim 14, further comprising:
applying a compressive force to the microvalve vessel occluder to move the microvalve vessel occluder from a non-deployed configuration to a deployed configuration before infusing.
26. The method of claim 25, wherein the microvalve vessel occluder includes a proximal end and a distal end, the microcatheter comprises a distal stop to limit travel of the distal end of the microvalve vessel occluder, and the compressive force is applied between the proximal end of the microvalve vessel occluder and the distal stop to expand the diameter of the microvalve vessel occluder.
27. A method of delivering a therapeutic agent to through a vasculature of a patient to a solid tumor in an organ, wherein the vasculature comprise a blood vessel and a plurality of branches from a network of distal blood vessels having a plurality of bifurcation, the method comprising:
- a) advancing a distal tip at a distal end of an infusion catheter into a target infusion location within one of the distal blood vessels, the infusion catheter extending from a proximal end to the distal end, the infusion catheter comprises a lumen extending from the proximal end to the distal end and opens at a distal orifice passing through the distal tip, wherein the distal blood vessel is in fluid communication with the solid tumor;
 - b) advancing an occluder distally over the infusion catheter to a target occlusion location in the blood vessel to partially occlude blood flow past the target occlusion location, wherein the occluder is longitudinally displaceable over the infusion catheter; and

c) infusing a fluid comprising a therapeutic agent through the lumen and out of the distal orifice of the infusion catheter and into the distal blood vessel,

wherein the target infusion location is at least one bifurcation distal of the target occlusion location in the blood vessel.

28. The method of claim 27, further comprising:

d) flushing the lumen of the infusion catheter with a flushing fluid at a flow rate that increases vascular pressure in a portion of the vasculature distal of the distal end of the catheter.

29. The method of claim 27, wherein the occluder is attached to a tubular member longitudinally displaceable over the infusion catheter, the method further comprising:

d) withdrawing the infusion catheter from the blood vessel through a lumen of the tubular member; and

e) flushing the lumen of the tubular member with a flushing fluid at a flow rate that increases vascular pressure in a portion of the vasculature distal of a distal end of the tubular member.

30. The method of claim 27, further comprising:

advancing a guidewire into the distal blood vessel to the target infusion location, before step a), wherein the infusion catheter is advanced into the distal blood vessel over the guidewire; and

removing the guidewire before step c).

31. The method of claim 27, further comprising,

d) advancing a distal end of a sensing wire through the lumen of the infusion catheter until the distal end of the sensing wire reaches a sensing location in the vasculature; and

e) flushing the lumen of the infusion catheter with a flushing fluid at a flow rate that increases vascular pressure in a portion of the vasculature distal of the distal end of the catheter.

32. The method of claim 27, further comprising

advancing a distal end of a sensing wire through the lumen of the infusion catheter until the distal end of the sensing wire reaches a sensing location in the vasculature, before step c), wherein the sensing wire measures a pressure in the vasculature during infusion of the fluid comprising the therapeutic agent.

33. The method of claim 27, wherein the fluid is infused at a flow rate that increases vascular pressure in a portion of the vasculature distal of the target occlusion location

34. The method of any one of claims 27-33, wherein the blood vessel is an artery and the network of distal blood vessels are a network of arterial vessels downstream of the artery.

35. The method of any one of claims 27-33, wherein the target infusion location is at least two bifurcations distal of the target occlusion location in the blood vessel.

36. The method of any one of claims 27-33, wherein the target infusion location is at least three bifurcations distal of the target occlusion location in the blood vessel.

37. The method of any one of claims 27-33, wherein the organ is selected from the group consisting of: liver, pancreas, kidney, spleen, prostate, uterus, small intestine.

38. The method of claim 37, wherein the organ is the liver.

39. A method of delivering a therapeutic agent to through a vasculature of a patient to a solid tumor in an organ, wherein the vasculature comprise a blood vessel and a plurality of branches from a network of distal blood vessels having a plurality of bifurcation, the method comprising:

a) advancing a tubular member and an occluder attached to an exterior surface of the tubular member into the blood vessel to a target occlusion location to partially occlude blood flow past the target occlusion location;

b) advancing a distal tip at a distal end of an infusion catheter through a lumen of the tubular member to a target infusion location within one of the distal blood vessels, the infusion catheter extending from a proximal end to the distal end, the infusion catheter comprises a lumen

extending from the proximal end to the distal end and opens at a distal orifice passing through the distal tip, wherein the distal blood vessel is in fluid communication with the solid tumor;

c) infusing a fluid comprising a therapeutic agent through the lumen of the infusion catheter and out of the distal orifice of the infusion catheter and into the distal blood vessel, wherein the target infusion location is at least one bifurcation distal of the target occlusion location in the blood vessel.

40. The method of claim 39, further comprising:

d) flushing the lumen of the infusion catheter with a flushing fluid at a flow rate that increases vascular pressure in a portion of the vasculature distal of the distal end of the catheter.

41. The method of claim 39, wherein the method further comprising:

d) withdrawing the infusion catheter from the blood vessel through the lumen of the tubular member; and

e) flushing the lumen of the tubular member with a flushing fluid at a flow rate that increases vascular pressure in a portion of the vasculature distal of a distal end of the tubular member.

42. The method of claim 39, further comprising:

advancing a guidewire into the distal blood vessel to the target infusion location, before step a), wherein the infusion catheter is advanced into the distal blood vessel over the guidewire; and

removing the guidewire before step c).

43. The method of claim 39, further comprising,

d) advancing a distal end of a sensing wire through the lumen of the infusion catheter until the distal end of the sensing wire reaches a sensing location in the vasculature; and

e) flushing the lumen of the infusion catheter with a flushing fluid at a flow rate that increases vascular pressure in a portion of the vasculature distal of the distal end of the catheter.

44. The method of claim 39, further comprising
advancing a distal end of a sensing wire through the lumen of the infusion catheter until the distal end of the sensing wire reaches a sensing location in the vasculature, before step c), wherein the sensing wire measures a pressure in the vasculature during infusion of the fluid comprising the therapeutic agent.
45. The method of claim 39, wherein the fluid is infused at a flow rate that increases vascular pressure in a portion of the vasculature distal of the target occlusion location
46. The method of any one of claims 39-45, wherein the blood vessel is an artery and the network of distal blood vessels are a network of arterial vessels downstream of the artery.
47. The method of any one of claims 39-45, wherein the target infusion location is at least two bifurcations distal of the target occlusion location in the blood vessel.
48. The method of any one of claims 39-45, wherein the target infusion location is at least three bifurcations distal of the target occlusion location in the blood vessel.
49. The method of any one of claims 39-45, wherein the organ is selected from the group consisting of: liver, pancreas, kidney, spleen, prostate, uterus, small intestine.
50. The method of claim 49, wherein the organ is the liver.
51. A treatment system for delivering a therapeutic agent within a vasculature of a patient, comprising:
a flexible microcatheter comprising a proximal end, a distal portion extending to a distal end, an outer diameter, and a lumen having an inner diameter extending from the proximal end to a distal orifice located at the distal end;
a flexible catheter comprising a proximal end, a distal portion extending to a distal end, an inner diameter, a lumen extending from the proximal end to a distal orifice located at the distal end and having an inner diameter; and

a microvalve vessel occluder attached to the flexible catheter.

52. The treatment system of claim 51, further comprising:
a flexible guidewire comprising a proximal end, a distal portion extending to a distal end, and an outer diameter.
53. The treatment system according to claim 51 or 52, further comprising:
a flexible sensing wire comprising a proximal end, a distal portion extending to a distal end, an outer diameter, and one or more sensing elements.
54. The treatment system according to claim 51 or 52, further comprising:
one or more radiopaque marker bands located on the flexible microcatheter or the flexible catheter.
55. The treatment system according to claim 52, further comprising:
one or more radiopaque marker bands located on the flexible guidewire.
56. The treatment system according to claim 53, further comprising:
one or more radiopaque marker bands located on the flexible sensing wire.