[0011] While diseases that cause damage to specific cells or tissues are clear candidates for cellular therapy, there remains a need in the art for methods, substrate, and tools to improve the efficacy of cellular therapy.

BRIEF SUMMARY

[0012] Cells to be used in or on the delivered substrate are cultured on a completely fabricated and sterilized substrate. Substrates as described herein may be sterilized by gamma irradiation, ethylene oxide, autoclaving, ultraviolet (UV) sterilization, or other known procedures without degradation or damage. Cells are introduced to the sterilized substrate under sterile cell culture or sterile surgical suite conditions. The advantages of such processes are that optimally healthy and robust cells of a specific type (e.g. mature, differentiated, etc.) can be selected and deposited onto the substrate just prior to implantation, or further grown on the substrate prior to implantation. By further growing cells on a substrate prior to implantation, the substrate quality can be assessed by viewing cell growth uniformity, maturation, etc. Upon confirmation of not only cell growth, but substrate quality, the cell seeded substrate may be shipped for short term implantation or can be cryopreserved for later thaw and use.

[0012a] According to a first aspect, there is provided an instrument for implantation of a flexible, ultra-thin substrate onto a target tissue, including: a handpiece; a tubular sheath extended in a distal direction from said handpiece; an internal shaft nested within said tubular sheath and anchored with said handpiece, wherein the internal shaft includes: a) a fixed tine that is parallel to the tubular sheath, the fixed tine having a clamp head; and b) a movable tine with a clamp head that is configured to move inwardly with respect to the clamp head of the fixed tine, the movable tine including an arch configured to variably interact with an inner wall of the tubular sheath and close the clamp heads to within a zero or predetermined distance from one another when the clamp heads retract inside the tubular sheath; a movement control mechanism configured to cause a longitudinal movement of said tubular sheath with respect to said handpiece and thus cause the arch to variably interact with the inner wall of the tubular sheath.

[0012b] According to a second aspect, there is provided a method of loading an instrument for implantation of a substrate, the method including: longitudinally actuating a tubular sheath in order to cause a variable contact interaction between an inner wall of the tubular sheath and a curvature of one or more flexible tines, causing at least one of the flexible tines to move and grasp a substrate; further longitudinally actuating the tubular sheath to induce a folding of the substrate; yet further longitudinally actuating a tubular sheath to slide the folded substrate within the tubular sheath.

[0012c] According to a third aspect, there is provided a method of using an instrument for implantation of a substrate, the method including: longitudinally actuating a tubular sheath in

a proximal direction in order to slide a folded substrate out of the tubular sheath; further longitudinally actuating the tubular sheath in a proximal direction to induce an unfolding of the substrate by removing an interaction between said substrate and said tubular sheath; yet further longitudinally actuating the tubular sheath in a proximal direction to cause a variable contact interaction between an inner wall of the tubular sheath and a curvature of one or more flexible tines, causing at least one of the flexible tines to move and release the substrate.

[0012d] According to a fourth aspect, there is provided a method of loading an instrument for implantation of a substrate, the method including: longitudinally actuating an internal shaft in order to cause a variable contact interaction between an inner wall of a tubular sheath and a curvature of one or more flexible tines, causing at least one of the flexible tines to move and grasp a substrate; further longitudinally actuating the internal shaft to induce a folding of the substrate; yet further longitudinally actuating the internal shaft to slide the folded substrate within the tubular sheath.

[0012e] According to a fifth aspect, there is provided a method of using an instrument for implantation of a substrate, the method including: longitudinally actuating an internal shaft in a distal direction to slide a folded substrate out of a tubular sheath; further longitudinally actuating the internal shaft in a distal direction to induce an unfolding of the substrate by removing an interaction with said substrate and said tubular sheath; yet further longitudinally actuating the internal shaft in a distal direction to cause a variable contact interaction between an inner wall of the tubular sheath and a curvature of one or more flexible tines located distally on the internal shaft, causing at least one of the flexible tines to move and release the substrate.

[0013] In certain embodiments, the cell seeded substrate may be loaded onto a unique surgical instrument (e.g. a surgical introducer) prior to cryopreservation and before subsequent implantation of the implant by a surgeon.

[0014] Substrates in accordance with embodiments described herein may be delivered by various methods depending on the target tissue, all of which would benefit from the use of specialized delivery devices according to the shape, size, thickness, cell type, and overall thickness of the cell seeded substrate. Substrates may be delivered during an open surgical process, endoscopically, intravascularly, intramuscularly, stereotactically, or by other means known in the field for the particular target tissue.

[0015] In several embodiments, there is provided an instrument for the implantation of a substrate for transplanting (or subsequent seeding with a biological tissue, such as cells, a multi-cell type solution, matrix, time release gel, microbubbles, or any other treatment vehicle that can be placed on, in, within or anchored to the substrate) into a target tissue of a subject, comprising a handpiece comprising a proximal end and a distal end, the distal end comprising an orifice, a distal tubular sheath extending in a distal direction from said