DEVICES, SYSTEMS, AND METHODS FOR THE FABRICATION OF TISSUE

REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation of U.S. application Ser. No. 13/968,313, filed Aug. 15, 2013, which is a continuation of U.S. application Ser. No. 13/246,428, filed Sep. 27, 2011, which claims the benefit of U.S. provisional App. Ser. No. 61/405,582, filed Oct. 21, 2010, each of which is incorporated by reference in its entirety.

BACKGROUND OF INVENTION

[0002] A number of pressing problems confront the healthcare industry. As of December 2009 there were 105,305 patients registered by United Network for Organ Sharing (UNOS) as needing an organ transplant. Between January and September 2009, only 21,423 transplants were performed. Each year more patients are added to the UNOS list than transplants are performed, resulting in a net increase in the number of patients waiting for a transplant. For example, at the beginning of 2008, 75,834 people were registered as needing a kidney; at the end of that year, the number had grown to 80,972. 16,546 kidney transplants were performed that year, but 33,005 new patients were added to the list. The 2008 transplant rate for a patient registered by UNOS as needing a kidney was 20%. The mortality rate of waitlist patients was 7%.

[0003] Additionally, the research and development cost of a new pharmaceutical compound is approximately $1.8 billion. See Paul, et al. (2010). How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nature Reviews Drug Discovery 9(3):203-214. Drug discovery is the process by which drugs are discovered and/or designed. The process of drug discovery generally involves at least the steps of: identification of candidates, synthesis, characterization, screening, and assays for therapeutic efficacy. Despite advances in technology and understanding of biological systems, drug discovery is still a lengthy, expensive, and inefficient process with low rate of new therapeutic discovery.

SUMMARY OF THE INVENTION

[0004] There is a need for tools and techniques that facilitate application of regenerative medicine and tissue engineering technologies to relieving the urgent need for tissues and organs. There is also a need for tools and techniques that substantially increase the number and quality of innovative, cost-effective new medicines, without incurring unsustainable R&D costs. Accordingly, the inventors describe herein devices, systems, and methods for fabricating tissues and organs.

[0005] Described herein are bioprinters comprising: one or more printer heads, wherein a printer head comprises a means for receiving and holding at least one cartridge, and wherein said cartridge comprises contents selected from one or more of: bio-ink and support material; a means for calibrating the position of at least one cartridge; and a means for dispensing the contents of at least one cartridge. In one embodiment, a printer head described herein comprises a means for receiving and holding one cartridge. In another embodiment, a printer head described herein comprises a means for receiving and holding more than one cartridge. In another embodiment, the bioprinter further comprises a printer stage. In another embodiment, the means for receiving and holding at least one cartridge is selected from: magnetic attraction, a collet chuck grip, a ferrule, a nut, a barrel adaptor, or a combination thereof. In yet another embodiment, the means for receiving and holding at least one cartridge is a collet chuck grip. In yet another embodiment, the means for calibrating the position of at least one cartridge of is selected from: laser alignment, optical alignment, mechanical alignment, piezoelectric alignment, magnetic alignment, electrical field or capacitance alignment, ultrasound alignment, or a combination thereof. In yet another embodiment, the means for calibrating the position of at least one cartridge is laser alignment. In another embodiment, the means for dispensing the contents of at least one cartridge is application of a piston, application of pressure, application of compressed gas, hydraulics, or a combination thereof. In yet another embodiment, the means for dispensing the contents of at least one cartridge is application of a piston. In yet another embodiment, the diameter of the piston is less than the diameter of a cartridge. In another embodiment, the bioprinter further comprises a means for adjusting temperature. In yet another embodiment, the bioprinter further comprises a means for adjusting the ambient temperature, the temperature of a cartridge, the temperature of the contents of the cartridge, the temperature of the receiving surface, or a combination thereof. In yet another embodiment, the means for adjusting temperature is a heating element. In yet another embodiment, the means for adjusting temperature is a heater. In yet another embodiment, the means for adjusting temperature is a radiant heater, a convection heater, a conductive heater, a fan heater, a heat exchanger, or a combination thereof. In yet another embodiment, the means for adjusting temperature is a cooling element. In yet another embodiment, the means for adjusting temperature is a container of coolant, a chilled liquid, ice, a radiant cooler, a convection cooler, a conductive cooler, a fan cooler, or a combination thereof. In yet another embodiment, the temperature is adjusted to between about 40 and about 90° C. In yet another embodiment, the temperature is adjusted to between about 0 and about 10° C. In another embodiment, a bioprinter disclosed herein, further comprises a means for applying a wetting agent to one or more of: the printer stage; the receiving surface, the deposition orifice, bio-ink, support material, or the printed construct.

[0006] Also disclosed herein are methods of calibrating the position of a cartridge comprising a deposition orifice, wherein the cartridge is attached to a bioprinter, comprising: calibrating the position of the cartridge along at least one axis; wherein the axis is selected from the x-axis, y-axis, and z-axis; and wherein each calibration is made by use of a laser. In one embodiment, the methods comprise activating the laser and generating at least one substantially stable and/or substantially stationary laser beam, and where said laser beam is horizontal to the ground. In another embodiment, the methods comprise activating the laser and generating at least one substantially stable and/or substantially stationary laser beam, and where said laser beam is vertical to the ground. In yet another embodiment, each calibration is made by use of first and a second laser. In yet another embodiment, the first laser is vertical to the ground and the second laser is horizontal to the ground. In another embodiment, calibrating the position of the cartridge along the y-axis by use of a horizontal laser comprises: positioning the cartridge so that the cartridge is (i) located in a first y octant