Emerging Medical Devices for Minimally Invasive Cell Therapy

Eoin D. O'Cearbhaill, PhD; Kelvin S. Ng, BS; and Jeffrey M. Karp, PhD

CME Activity

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Learning Objectives: On completion of this article, you should be able to (1) identify the challenges faced in designing devices for minimally invasive cell therapy, (2) recognize the common approaches in the minimally invasive delivery of cell therapy to cardiac tissue, (3) identify the proposed methods and benefits of macroencapsulation devices in the treatment of type 1 diabetes.

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From the Department of Medicine, Center for Regenerative Therapeutics, and Department of Medicine, Division of Biomedical Engineering, Brigham and Women's Hospital, Harvard Medical School, Boston, MA (E.D.O., K.S.N., J.M.K.); Harvard Stem Cell Institute, Cambridge, MA (E.D.O., K.S.N., J.M.K.); Harvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA (E.D.O., K.S.N., J.M.K.); and School of Mechanical and Materials Engineering, University College Dublin, Dublin, Ireland (E.D.O.).

Abstract

The past decade has seen the first wave of cell-based therapeutics undergo clinical trials with varying degrees of success. Although attention is increasingly focused on clinical trial design, owing to spiraling regulatory costs, tools used in delivering cells and sustaining the cells' viability and functions in vivo warrant careful scrutiny. While the clinical administration of cell-based therapeutics often requires additional safeguarding and targeted delivery compared with traditional therapeutics, there is significant opportunity for minimally invasive device-assisted cell therapy to provide the physician with new regenerative options at the point of care. Herein we detail exciting recent advances in medical devices that will aid in the safe and efficacious delivery of cell-based therapeutics.

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Cell-based therapeutics represent the third and newest pillar of medicine, after small-molecule drugs and biological agents.[1] As environment-responsive manufacturers of small molecules and biological agents, cells can naturally, or be engineered to, invoke reparative responses; unlike small molecules and biological agents, cells can additionally replace anatomical or functional defects and, ultimately, regenerate or restore tissue function. Through advancements in culture methods for reprogramming, differentiating, and expanding cells, the clinician can now potentially be armed with an array of cell populations with almost any phenotype. Whereas quality control and safety assurance of exogenous cell populations are challenges pertinent to the success of cell therapy,[2] a less commonly appreciated challenge is the accuracy and reproducibility in administering donor cells to the correct anatomical location with sufficient retention, engraftment, and survival for therapeutic efficacy. Cell-based therapeutics can act locally or systemically,[3-5] and clinicians require tools to tailor the action of

transplanted cells in a consistent and disease-specific manner. Through improved delivery of cell-based therapeutics, minimally invasive device-assisted approaches may help minimize variability in outcomes and provide a safer means to administer regenerative medicine. Medical device innovations can also help with challenges associated with harvesting, capturing, and isolating cells in sufficient numbers for therapy, as reported elsewhere.[6-8] Herein, we describe the current state of the art of infusion and encapsulation devices for minimally invasive delivery of cell-based therapeutics. For the purposes of this review, we focused on specific areas of promise for cell therapy, namely, cardiovascular disease and type 1 diabetes (T1D).

CELL INFUSION: NOT JUST ANOTHER DRUG

With the advent of cell-based therapeutics, there has been a tendency to rely on existing delivery platforms, such as the traditional needle and syringe[9] or the balloon-dilating catheter,[10] which may be poorly equipped to deliver their fragile cargo. Multiple routes of cell delivery have been used or proposed: oral, inhalation, topical, intravascular, intramuscular, subcutaneous, intraperitoneal, rectal/vaginal, transluminal via a natural orifice, and more tissue-specific routes (eg, intrathecal, intraventricular, and intra-articular). Although these routes are routinely used for conventional therapeutics, some (eg, oral and inhalation) expose cells to harsh environments owing to the body's defense barriers and are generally not suitable for cell delivery. Injection of cell-based therapeutics through skin or mucosa bypasses some barriers and can additionally facilitate delivery to a specific site or to a secondary site where cells can actively migrate or be passively transported to reach target sites. Figure 1 illustrates common routes and sites of cell delivery.

A commission report by the Pharmaceutical Research and Manufacturers of America offers insight into recent trends in cell therapy administration.[11] The report highlights a small subset of current cell therapies undergoing clinical trials or being reviewed by the Food and Drug Administration in early 2013. Through analyzing this report and data available on ClinicalTrials.gov

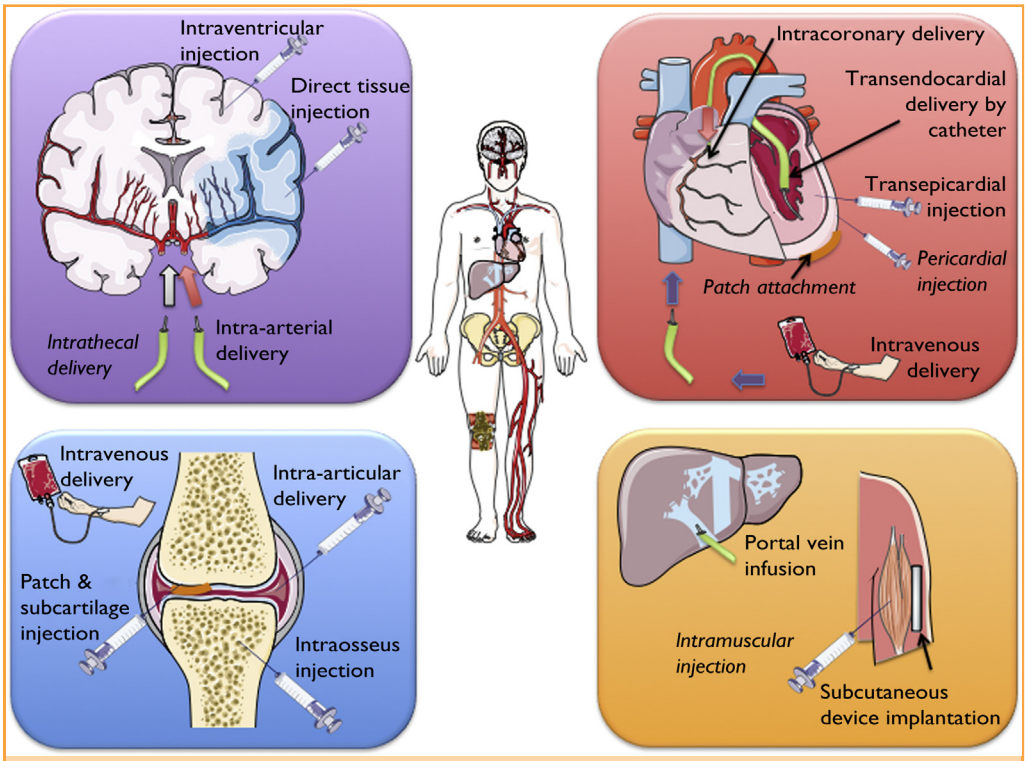

FIGURE 1. Current and proposed (in italics) injection sites and methods for cell therapy. The delivery methods highlighted are for minimally invasive (clockwise from top left) neural, cardiovascular, diabetes, and orthopedic cell therapy. Images adapted from Servier Medical Art.

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