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Regenerative Medicine for Radiation-induced Vascular Disease

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Experimental studies in animals have established a causal relationship between irradiation and vascular disease. Clinical studies indicate that patients who have previously undergone radiation therapy for various malignancies such as lymphoma, breast cancer, and head and neck cancer are at increased risk for developing vascular disease. Depending on the radiation exposure dose, hematopoietic (2-10 Gy), gastrointestinal (>10 Gy) and neurocardio-vascular syndromes (>30 Gy) can occur. Experimental studies in vitro and in vivo indicate that radiation therapy causes acute up-regulation of pro-inflammatory cytokines, chronic oxidative stress and adhesion molecules in endothelium that recruits inflammatory cells to sites of vascular injury. Cell therapy for angiogenesis using bone-marrow mononuclear cells (BM-MNCs) in patients with peripheral arterial disease (PAD) was the first successful trial for human patients. Endothelial progenitor cells (EPCs) that are derived from bone marrow, as well as circulating progenitor cells, have surface markers such as CD34+ /AC133+ /Tie2. These cells differentiated into vascular endothelial cells. In animal models of ischemia, heterologous, homologous and autologous EPCs were incorporated into sites of active angiogenesis. PAD is associated with endothelial dysfunction and cellular injury to the blood vessels leading to tissue ischemia. Therefore, it is clinically important to evaluate the vascular function of collateral arteries induced by BM-MNC implantation. BM-MNC implantation has been shown to induce therapeutic angiogenesis in both ischemic limb models and patients with limb ischemia. To provide comprehensive options for patients with radiation-induced vascular disease, various angiogenic approaches, including induced mesenchymal stem cell therapy, gene therapy and regenerative medicine therapeutic medical devices, have been tried for revascularization of ischemic tissues in animal models of ischemia for future translational medicine.

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