Type 1 Diabetes (T1D) results from the autoimmune destruction of β-cells within the pancreatic islets. Current patient care management, i.e. exogenous insulin, supplemental agents, and dietary regulation is unable to prevent long term complications. Clinical trials have demonstrated the potential to eliminate diabetic symptoms by cell therapy using transplanted islets. However, transplantation of donor islets is greatly limited by immunogenic responses and delayed integration with the recipient’s vasculature. Mesenchymal stem cells (MSC) are dynamic cells capable of robust immunomodulatory and vasculogenic effects. MSC mediate the surrounding environment and respond to molecular cues with a robust, comprehensive secretory profile specific to the needs of the milieu. We propose heterotopic islet spheroids containing islets, MSC, and endothelial cells as an attractive transplantable construct that rapidly assembles, generates internal vasculature, and enhances vasculogenic processes post-transplantation. Vascular beds are prepared by self-assembly of endothelial cells which serve as the transplantation site. Recently, the Taniguchi and Takebe groups corroborated the heterotopic islet spheroid in vivo, demonstrating improved islet survival attributed to enhanced vasculogenesis after transplantation. Here, we developed an in vitro model to assimilate transplantation of heterotopic islet spheroids onto vasculature which provide valuable insight into cellular processes and signaling to further investigate the use of these islet constructs as a prospective cell transplantation strategy. This model permits time-lapse imaging of vascular cell recruitment, cellular re-organization within the spheroids, and collection of secreted insulin and immunomodulatory and angiogenic mediators. Following transplantation, cells from the vasculature were recruited and integration within the construct subsequently revealed pinwheel-like structures suggesting vasculogenesis was achieved. Together, this evidence validates a promising cell transplantation strategy mediated by MSC for enhanced vasculogenesis.