

# Are Autologous Tissue-Engineered Blood Vessel Substitutes Feasible? Where Do We Stand with This Holy Grail?

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*Bauer E. Sumpio, MD, PhD, New Haven, CT*

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There is a tremendous impetus in the vascular community to develop synthetic small-diameter grafts that have high long-term patency rates. "Off the shelf" availability in various diameters and lengths, uncomplicated storage or preparation requirements, and easy handling are the main advantages of such grafts, whereas their inherent thrombogenicity and compliance mismatch are their main drawbacks. Synthetic grafts have been associated with excellent long-term results in treating the pathology of large diameter arteries, where the flow is high and the resistance low; the patency rates have been disappointing when they are used to replace small diameter (< 6 mm) arteries, such as the coronary and the infragenicular vessels.

One strategy to overcome these limitations employs the application of tissue engineering techniques to construct biological substitutes of diseased native vessels. These artificial blood vessels should ideally be composed of viable tissues, able to contract in response to hemodynamic forces and chemical stimuli and secrete normal blood vessel products. Artificial blood vessels should also allow complete healing without any immunologic reaction, remodeling according to the needs of the environment and even have the ability to grow when placed in children. Compliance, lack of thrombogenicity, and resistance to infections are theoretic advantages of such grafts, whereas burst strength and "off the shelf" availability are additional desirable goals.

Three basic elements are generally required for the construction of an artificial vessel: a scaffold, cells, and an appropriate nurturing environment. The purpose of the scaffold is to provide a temporary skeleton to support the growing tissue and provide the desired shape until the cells produce their own extracellular matrix (ECM). Two main types of scaffolds have been utilized: collagen matrices and biodegradable polymers. Another strategy is to use a tubular mandrel as a supporting device in vitro and remove it prior to implantation of the graft to the host. Autologous or allogeneic smooth muscle cells (SMC), fibroblasts and endothelial cells (EC) can then be seeded on the scaffold and cultured until a cellularized vessel with strong mechanical properties is created. A bioreactor mimicking the in vivo environment of the vascular cells by producing pulsatile flow has proven quite useful in this process.

Initial results show that the construction of an artificial vessel combining desirable biologic and mechanical characteristics is feasible. The incorporation of recent advances in molecular and genetic engineering to the already developed techniques is expected to aid in the solution of the problems that have emerged. The clinical imperative for better vascular grafts, the great scientific challenge and the large commercial opportunity for such a graft guarantee that significant developments are to be anticipated in this field in the near future.

## References

1. Kakisis JD, Liapis CD, Breuer C, Sumpio BE. Artificial blood vessel: the holy grail of peripheral vascular surgery. *J Vasc Surg* 2005;41:349-54.