Commentary

The surgical repair of congenital cardiac defects, including relief of stenotic lesions and reconstruction of complex cardiac anomalies, often requires patch reconstruction or placement of a synthetic conduit. Although a number of graft materials are available for use in these applications, the long-term results of reconstructive procedures with these materials are limited by their lack of growth potential, thrombogenicity, and lack of contractility. The ideal graft material would have growth potential, be nonthrombogenic, and be able to contract synchronously with surrounding normal myocardium if used to replace a portion of the right or left ventricle. Graft materials composed of viable cellular element within a biodegradable scaffold that can undergo remodeling or absorption may best meet these criteria. Patches and conduits with these properties, once implanted, might not require repeated re-replacement as the child grows, a limitation that currently results in significant morbidity and mortality.

A number of research groups have been involved in the development of new materials with potential cardiovascular applications. Dr Mayer's laboratory has been one of the pioneers in the development of tissue-engineered heart valves and pulmonary artery conduits. Their previous studies have demonstrated that vascular cells can be seeded into, and grown in, different biodegradable materials. These tissue-engineered materials may be used to construct valve leaflets and vascular conduits. In this study, Stock and colleagues¹ report the *in vivo* behavior of patches composed of a rapidly degraded biopolymer, poly-4-hydroxybutyric acid (P-4HB), into which ovine vascular cells were seeded. These autologous cell-seeded patches were implanted into the pulmonary artery of the original donor animal. Histologic examination of these patches at up to 6 months demonstrated near-complete resorption of the P-4HB substrate and formation of organized tissue by the seeded cells. Increasing cellular and extracellular matrix content of the seeded patches suggested proliferation and synthetic activity of the cells within the graft.

We have examined the 3-dimensional growth characteristics of rat cardiomyocytes, smooth muscle cells, and endothelial cells, as well as human heart cells, when seeded into a biodegradable gelatin mesh. These cells can proliferate within the gelatin substrate, forming tissue.² Thicker grafts may be constructed by layering several grafts together, but the dependence of the

seeded cells on passive diffusion for oxygen and nutrient delivery remains a limiting factor in the *in vitro* construction process before implantation. We have also grown fetal rat cardiomyocytes in a similar mesh. These cardiomyocytes proliferated and formed a spontaneously rhythmically contractile graft that survived and contracted both *in vitro* and *in vivo*.³

A number of issues, however, remain to be resolved. These include the determination of the optimal number, cell type, and mixture of cell types to be seeded, as well as the length of time required for *in vitro* generation of these grafts before implantation, which affects clinical utility. The optimal biodegradable substrate has yet to be determined, both for support of graft cellular elements and for ease of handling during surgical implantation. The long-term behavior of these grafts must also be evaluated. Stock and colleagues¹ noted bulging of the unseeded biopolymer graft after 20 weeks, perhaps representing the beginning of aneurysmal dilatation. We have noted similar findings in cell-seeded gelatin grafts implanted into the right ventricular outflow tract of rats. Over the limited duration of these experiments, cell-seeded patches did not appear to dilate in the same manner as unseeded patches. Longer follow-up will be required, however, to determine whether late aneurysmal dilation, particularly when the graft is subjected to higher pressures and stresses in the left-sided circulation, will become a liability of these materials.

These types of tissue-engineered grafts may in the future become the ideal materials for the surgical repair or palliation of congenital cardiac defects. Ultimately, these grafts may offer the promise of a single operation that will last the patient indefinitely, reducing the morbidity and mortality and improving the quality of life of these children.

*Ren-Ke Li, MD, PhD
Terrence M. Yau, MD, MSc
Toronto, Ontario, Canada*

REFERENCES

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