

Joseph W. Turek, MD, PhD, MBA
Duke University Medical Center

Partial Heart Transplantation: A Growing Solution for Pediatric Valve Disease

Congenital heart valve disease remains one of the most challenging problems in pediatric cardiac surgery. For decades, surgeons have relied on mechanical valves, bioprostheses, and cryopreserved homografts. These options that offer reliability in adults but fall short in infants and young children who need valve replacements capable of growing with them. Reinterventions are the rule, not the exception, and the cumulative operative risk, anticoagulation burden, and risk of structural deterioration all compound over a child's lifetime.

Partial heart transplantation (PHT) has emerged over the past several years as an innovative strategy designed to fill this longstanding gap. By transplanting living valve and root tissue from a donor and maintaining cellular viability through limited immunosuppression, PHT seeks to replicate the biological behavior of a native valve which includes the capacity for somatic growth and adaptive remodeling. What began as a solution for critically ill neonates with truncal valve disease is now evolving into a broader platform with applications across congenital heart surgery, heart transplantation, and even adult valve disease. Although early in its clinical development, PHT is rapidly moving from a compelling idea to a reproducible reality.

This article provides an overview of the current state of PHT, integrating published experience in humans, emerging applications such as the "living Ross" and mitral PHT, and multicenter adoption.

Rationale for Partial Heart Transplantation

The concept of replacing valve tissue while maintaining viability is not new. Early attempts at "homovital" homografts delivered fresh valve roots with encouraging early function, but without immunosuppression or modern preservation techniques, these implants inevitably lost viability. Advances in pediatric heart transplantation, cold ischemia tolerance, and immunologic understanding have now made living valve transplantation both biologically and clinically feasible.

PHT leverages several key biologic principles:

1. **Relative immune privilege of valve tissue.** Rejection predominantly targets myocardium, not valve endothelium or matrix, meaning valve-only transplantation may require much less immunosuppression.
2. **Living tissue grows.** Pediatric heart transplant recipients experience somatic growth of their donor organs. Transplanting a living valve offers the same potential.
3. **Cold-preserved valve roots maintain cellular viability** far longer than previously appreciated, creating flexibility in graft use and transport.

Together, these principles support the central premise of PHT: a living graft capable of remodeling and growing with the patient while requiring less immunosuppression than a full orthotopic heart transplant.

Clinical Experience: Semilunar PHT in Children

The first-in-human partial heart transplant, performed in 2022, marked a pivotal moment for congenital heart surgery.[1] Since then, the early clinical experience has expanded and is best summarized in a recent case series describing 19 patients.[2]

This cohort includes infants, older children, and adults, with the largest experience in aortic and pulmonary root PHT. Several variants including primary root replacement, domino grafts, and split-root implantation have been adapted to the needs of each patient and available donor tissue.

Across these diverse applications, several consistent findings have emerged:

- **Excellent early function.** No cases of early structural valve failure or major leaflet dysfunction have been reported within the initial follow-up periods.
- **Evidence of true somatic growth.** Infants demonstrated substantial increases in annular diameter and leaflet length, tracking appropriately with expected z-score growth curves.
- **Minimal immunosuppression suffices.** Most patients transitioned to tacrolimus monotherapy after the first month. One patient, who discontinued all immunosuppression for unrelated reasons, continued to demonstrate growth and preserved function.

These findings validate the fundamental rationale for PHT and suggest durability and growth potential beyond any previous valve substitute.

Global Adoption and Early Multicenter Experience

One of the strongest signals that PHT is maturing from an experimental concept to a reproducible platform is its rapid adoption across centers. Within the last three years, PHT has been performed at more than a dozen programs across the United States and Europe.

U.S. centers performing PHT include:

- Duke University
- Columbia University
- Boston Children’s Hospital
- Medical University of South Carolina
- Dell Children’s Medical Center / UT Austin
- Loma Linda University Children’s Hospital
- Children’s National Hospital
- Washington University / St. Louis Children’s Hospital
- Cincinnati Children’s Hospital
- Rady Children’s Hospital

European centers include:

- Geneva University Hospital, Switzerland
- Gregorio Marañón General University Hospital, Madrid, Spain

This breadth of adoption demonstrates:

- Technical reproducibility across diverse congenital programs,
- Growing comfort with immunosuppression-light strategies, and
- Broad applicability across various congenital pathologies and age groups.

The number and geographic diversity of programs now performing PHT is itself an important early outcome, one that reflects both the feasibility of the operation and the unmet need it seeks to address.

Organ Stewardship: Domino and Split-Root PHT

PHT also introduces new strategies for donor stewardship and valve availability.

Domino grafts
Valves explanted from heart transplant recipients, previously discarded, can now be used as viable grafts for children requiring PHT. This has dramatically expanded donor access and is used in most PHT cases.

Split-root grafts
A single donor heart may be divided into an aortic and pulmonary root, each used for a separate PHT recipient. This mirrors split-liver transplantation and represents a powerful method to increase the utility of each donor organ.

Expanding Indications: The Living Ross Procedure
The Ross procedure remains an attractive operation for children and young adults requiring aortic valve replacement, offering survival comparable to the age-matched general population. However, homograft degeneration in the RV-PA position remains a major limitation.

The “Living Ross” integrates PHT into the Ross procedure by using a living pulmonary root from a donor instead of a cryopreserved homograft.[3] If long-term data confirm improved durability, the Living Ross may redefine the standard for pediatric aortic valve disease, combining the advantages of the Ross with the biologic benefits of PHT.

Beyond Semilunar Valves: Atrioventricular PHT

Although the semilunar valves have been the first clinical frontier, the need for growth-capable mitral valve replacement is urgent. Mechanical valves in infants carry high morbidity, and multiple reoperations are expected.

A recent in vivo porcine study demonstrated that atrioventricular PHT is not only feasible but biologically active.[4] Gross pathology showed healthy tissue integration without calcification. This has now been translated to human mitral PHT at two centers in the US.

Immunologic Considerations

Optimal immunosuppression for PHT is still being refined, but early observations suggest a far lower immunologic burden than orthotopic heart transplantation.

Key emerging themes include:

- Tacrolimus monotherapy appears sufficient for most patients,
- DSA formation has not clearly correlated with graft dysfunction

The ability to maintain valve viability with minimal immunosuppression may ultimately become one of the most important advantages of PHT.

The Road Ahead

Partial heart transplantation is rapidly evolving from a novel solution for newborns with truncal valve disease into a broader platform. The early multicenter adoption across the U.S. and Europe underscores its feasibility, while its application in the atrioventricular position points to future expansion into the most challenging domains of pediatric valve replacement.

For cardiac surgeons and cardiologists, PHT represents a biological, technical, and conceptual shift. PHT is a living valve replacement strategy with the potential to reshape valve replacement for decades to come.

References

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