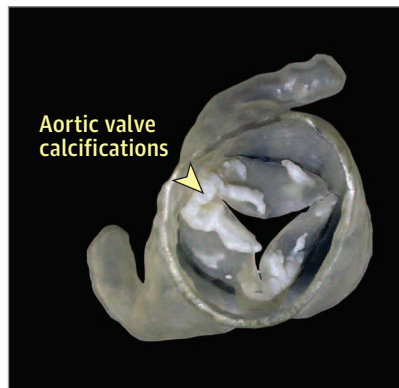


## Biotech Innovations

### Fit-Testing Transcatheter Aortic Valve Replacements With 3-D Printing

For patients with aortic valve stenosis who can't undergo open-heart surgery or who have a high risk of surgical complications, transcatheter aortic valve replacement (TAVR) is an increasingly popular minimally invasive alternative. Preprocedural fit-testing of TAVR valves using 3-dimensional (3-D) printing could one day help physicians choose the best device size for individual patients.



In a new workflow recently described in the *Journal of Cardiovascular Computed Tomography*, anatomical data from cardiac computed tomographic (CT) angiograms are used to guide multimaterial 3-D printing of a patient's aortic root and valve, including valvular atherosclerotic calcifications. The physical replica is then used to test which TAVR valve is most appropriate for that patient by employing a custom 3-D-printed sizing device.

A retrospective study of 30 patients who underwent TAVR at Massachusetts General Hospital found that "best fit" valve sizes predicted by the novel workflow were significantly correlated with gold-standard radiologist-conducted CT measurements.

The workflow correctly predicted the adequateness of the seal in 73.3% of patients who received a balloon-expandable valve and 60% patients who received a self-expanding valve.

"[T]he discordant cases were overwhelmingly ones in which there was a [paravalvular leak] known to result from

a suboptimal valve fit," said senior author Beth Ann Ripley, MD, PhD, an assistant professor in the radiology department at the University of Washington and the VA Puget Sound Health Care System in Seattle.

Her team discovered that depending on the size and location of calcified deposits, the replacement valve might not form a tight seal with the native damaged valve, arguing for surgery instead of TAVR.

The workflow still needs validation, including prospective studies, according to Ripley. The researchers are also working on new versions of the workflow for left atrial appendage occlusion and mitral valve procedures.

### Liver and Lung Transplant Advances

Every year, approximately 2400 people in the United States die while waiting for a liver transplant. A study published in the *American Journal of Transplantation* suggests that a new machine learning-based mortality predictor could help reduce those deaths.

Since 2002, donor livers have been allocated on a "sickest first" policy using the Model for End-Stage Liver Disease (MELD) score, which is based on 3 laboratory values. But the calculation doesn't accurately capture some patients' disease severity or progression, creating inequities and undesirable outcomes.

The new method, dubbed the Optimized Prediction of Mortality (OPOM), uses machine learning trained on the Standard Transplant Analysis and Research data set to predict the likelihood that a candidate will die or be removed from the waitlist within 3 months.

In the recent study, the OPOM more accurately predicted a liver candidate's death or removal from the list than MELD. The OPOM factors in as many as 28 laboratory values and their associated fluctuations over time. Importantly, the study found that female candidates and other subgroups currently disadvantaged by the MELD score would experience fewer waitlist deaths and more transplants using the OPOM allocation. However, the model's ability to predict outcomes

must still be validated in an independent data set, according to *JAMA* Deputy Editor Ed Livingston, MD.

In the future, the new method could potentially be used in other solid organ transplant populations, such as heart, kidney, and lung, "which also face the same dilemma of allocating a scarce resource to a growing population in need," said senior author Parsia Vagefi, MD, chief of surgical transplantation at the University of Texas Southwestern Medical Center in Dallas.

In other transplant news, researchers at the Genomic Research Alliance for Transplantation at the National Institutes of Health (NIH) recently described the first test that identifies patients at risk of developing chronic lung transplant rejection and allograft failure.

The proof-of-concept study, published in *EBioMedicine*, involved 106 lung transplant recipients whose plasma levels of donor-derived cell-free DNA (ddcfDNA) were measured in the first 3 months after the procedure. Over the next 3 years, patients with the highest average ddcfDNA levels soon after the transplant went on to have a 6.6-fold greater risk of developing chronic rejection and allograft failure than those with lower levels. Allograft failure was defined as severe chronic lung allograft dysfunction, retransplantation, and/or death from respiratory failure.

At the time of ddcfDNA testing, only a third of patients with high levels had clinical manifestations of allograft dysfunction. The other two-thirds had clinically silent dysfunction but later developed manifestations, according to Sean Agbor-Enoh, MD, first author of the study and codirector of the Laboratory of Transplantation Genomics at the NIH.

When diagnosed with allograft dysfunction using current clinical tools, patients ultimately die within 2 to 3 years. The new blood test could alert physicians to early disease, when interventions like tailored immunosuppressants, antibiotics, or phototherapy might be more effective, Agbor-Enoh added. — Jennifer Abbasi

**Note:** Source references are available online through embedded hyperlinks in the article text.