Pilot study suggests artificial intelligence could help assess, improve heart transplant outcomes

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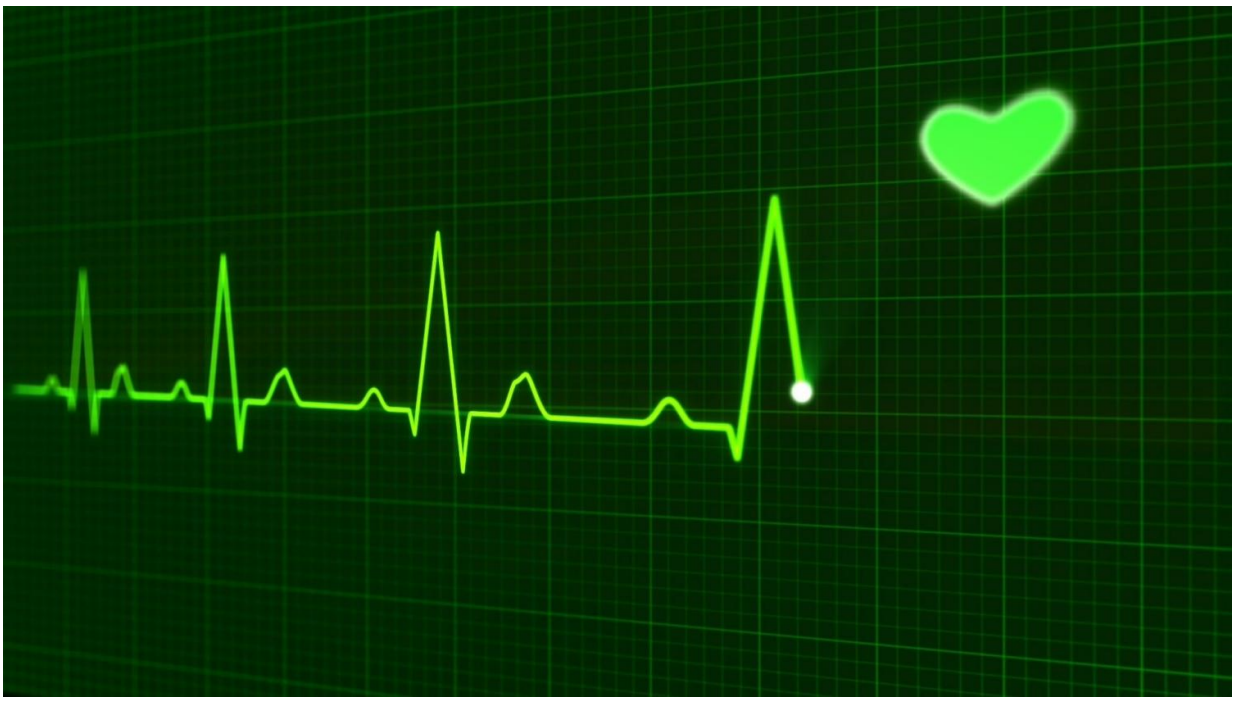

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Heart transplantation can be a lifesaving operation for patients with end-stage heart failure. However, many patients experience organ transplant rejection, in which the immune system begins attacking the transplanted organ. But detecting transplant rejection is challenging—in its early

stages, patients may not experience symptoms, and experts do not always agree on the degree and severity of the rejection. To help address these challenges, investigators from Brigham and Women's Hospital created an artificial intelligence (AI) system known as the Cardiac Rejection Assessment Neural Estimator (CRANE) that can help detect rejection and estimate its severity. In a pilot study, the team evaluated CRANE's performance on samples provided by patients from three different countries, finding that it could help cardiac experts more accurately diagnose rejection and decrease the time needed for examination. Results are published in *Nature Medicine*.

"Our retrospective pilot study demonstrated that combining artificial intelligence and human intelligence can improve expert agreement and reduce the time needed to evaluate biopsies," said senior author Faisal Mahmood, Ph.D., from the Mahmood Lab at the Brigham's Department of Pathology. "Our results set the stage for large-scale clinical trials to establish the utility of AI models for improving heart transplant outcomes."

Heart biopsies are commonly used to identify and grade the severity of organ rejection in patients after heart transplantation. However, several studies have shown that experts often disagree on whether the patient is rejecting the heart or on the degree of severity of the rejection. The variability in diagnosis has direct clinical consequences, causing delays in treatment, unnecessary follow-up biopsies, anxiety, inadequate medication dosing, and, ultimately, worse outcomes.

CRANE is designed to be used in tandem with expert assessment to establish an accurate diagnosis faster, and it can also be used in settings where there may be few pathology experts available. The team trained CRANE for detection, subtyping, and grading of transplant rejection using thousands of pathology images from over 1,300 heart biopsies from the Brigham. The researchers then validated the model, using test

biopsies from the Brigham and independent, external test sets received from hospitals in Switzerland and Turkey. The external validation datasets were constructed to demonstrate a large degree of variability to stress-test the proposed AI model.

CRANE performed well in detecting and assessing rejection, with results comparable to those from conventional assessments. When experts used the tool, it reduced disagreement between experts and decreased assessment time. The authors note that its use in clinical practice remains to be determined and plan to make further improvements to the system, but the results illustrate the potential of integrating AI into diagnostics.

"Throughout the history of medicine, diagnostic assessments have been largely subjective," said Mahmood. "But because of the power and assistance of computational tools, that's beginning to change. The time is right to make a shift by bringing together people with clinical expertise and those with expertise in computational science to develop assistive diagnostic tools."

More information: Faisal Mahmood, Deep learning-enabled assessment of cardiac allograft rejection from endomyocardial biopsies, *Nature Medicine* (2022). DOI: 10.1038/s41591-022-01709-2. www.nature.com/articles/s41591-022-01709-2

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