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CHALLENGES IN POST-RENAL TRANSPLANTATION MONITORING

Complex Protocols

- Surveillance options for allograft injury monitor biomarkers of injury, e.g., serum creatinine, proteinuria, donor-specific antibody (DSA), and BK virus.
- These markers may indicate graft injury too late which can lead to loss of graft, reduced quality of life, the need for repeat transplant, and high economic burden.

THERE IS A GLOBAL SHORTAGE OF ORGANS AVAILABLE FOR DONATION.

EVERY ORGAN COUNTS.

Early, Frequent Monitoring

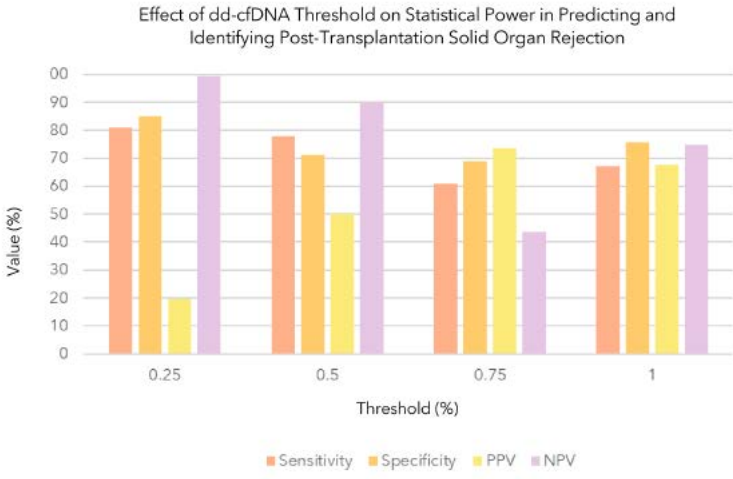
With a global shortage of organs available for donation, there is a significant benefit in using rejection detection methods that maximize post-operative success and improve patient quality of life. Implementing early and frequent monitoring ensures that rejection is identified swiftly and reliably, both improving outcomes and saving lives.

CFDNA: A CLOSER LOOK

During cell death, intracellular DNA is released into the bloodstream at which point it is called cell-free (cf) DNA. cf-DNA has been used an an effective analyte in maternal-fetal medicine and oncology. In organ transplant recipients, cell injury and death within the transplanted organ produces donor-derived (dd) cf-DNA, a newly useful analyte to detect allograph injury and rejection. dd-cfDNA is cleared from circulation within 15-90 minutes of release from the cell; thus, it is a virtually immediate read-out of graft status.

In order to quantify the extent to which cell death is occurring, dd-cfDNA must be differentiated from the recipient's own cfDNA. Methods exist to differentiate between donor and recipient DNA that exploit, genetic variation between individuals, e.g., single-nucleotide polymorphisms (SNPs) and insertions and/or deletions (indels).

DETERMINATION OF THRESHOLDS IN DD-CFDNA DETECTION



Various studies have sought to determine the optimal threshold for dd-ctDNA in detecting allograft rejection. The graph above and corresponding data table summarize the findings of several key publications. Results vary by study, and are influenced by factors such as type of rejection and sample size. Zhang et al. (2020) report the optimal threshold to be 0.25; Bu et. al (2021) report a threshold of 0.5%; and Murad et al. (2022) report 0.75%, which varying effects on power. The data corresponding to a threshold of 1.0% represent mean findings of Zhang et al., Bu et al., Murad et al., and Huang et al. (2019).

dd-cfDNA Threshold (%)	0.25	0.5	0.75	1.0
Sensitivity (%)	81.0	78	61.02	67.05
Specificity (%)	85.0	71.0	69.05	75.71
PPV (%)	19.6	50.0	73.47	67.64
NPV (%)	99.2	90.0	43.4	74.7