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Buying days, not merely hours: Isochoric supercooling and the next frontier of kidney preservation

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Kidney transplantation is often described as a problem of organ scarcity, but scarcity is only part of the problem. Donated kidneys are also perishable resources moving through a time-critical network. Once procurement interrupts blood flow, metabolism slows but does not stop, and ischemic injury accumulates. Static cold storage (SCS) at approximately 4 °C remains simple, inexpensive, and widely used, yet every additional hour constrains allocation, transport, assessment, and operating-room logistics. The central question in organ preservation is therefore not only how to keep a graft alive, but how to create enough time to use it well (Figure 1).

A recent MIT Technology Review report brought renewed attention to an isochoric supercooling platform that stored porcine kidneys at -4 °C without freezing or adding conventional cryoprotectants.[1] According to the report, kidneys preserved for 24, 48, or 72 h were rewarmed and autotransplanted, with recovery of urine production and biochemical function; one graft was reported to remain healthy at 200 days. An earlier 2026 conference abstract from the same broader research programme described a single porcine kidney that sustained life for 30 days after multiday supercooling, autotransplantation, and subsequent contralateral nephrectomy.[2] Separately, peer-reviewed evidence from an independent Canadian team showed that porcine kidneys could undergo 24-48 h of subzero storage using a distinct protocol before autotransplantation, with 7-day functional and histological outcomes comparable to static cold storage.[3] Importantly, the headline 72-h results remain available only through news reporting and conference-level disclosure and have not yet been reported in a complete peer-reviewed study.[1,2] Taken together, these observations mark an important transition: subzero kidney preservation is moving from ex vivo feasibility toward functional testing in large-animal transplant models.

The conceptual appeal is clear. Lower temperature suppresses metabolic demand, but ordinary freezing is destructive because ice nucleation and growth can disrupt membranes, extracellular architecture, and the microvasculature. Supercooling instead maintains the preservation solution in a metastable, ice-free liquid state below its equilibrium freezing point. Under isochoric conditions, the organ and solution are sealed in a rigid chamber without a bulk gas phase, changing both the thermodynamics and kinetics of ice formation.[4] Pressure can be monitored as an indicator of phase change, but the key design principle is constant volume rather than the application of a simple constant external pressure. This distinction matters because the innovation is not merely a colder ice box; it is a controlled physical environment intended to stabilize a state that is intrinsically vulnerable to nucleation.

Avoiding nonphysiological cryoprotectants could be a major translational advantage. Conventional cryopreservation strategies often require agents that must enter complex tissue uniformly, prevent ice at multiple scales, and then be removed without osmotic or chemical injury. Isochoric supercooling uses familiar organ-preservation solutions and aims for a more modest temperature reduction, trading the prospect of indefinite storage for a clinically meaningful extension from hours to days.

If reproducible, a 72-h preservation window could change transplantation at several levels. More time could permit better donor-recipient matching, confirmatory biopsy or molecular assessment, and deliberate acceptance of kidneys that are now declined because teams cannot resolve uncertainty quickly enough. Transport could become less dependent on chartered flights and overnight surgical schedules, potentially improving access for geographically remote centers. A longer window could also allow organs to be redirected after an unexpected recipient problem rather than discarded. Most importantly, preservation could become an enabling platform for quality assessment and treatment rather than a passive race against the clock.

Supercooling should not, however, be framed as a competitor that makes machine perfusion obsolete. Hypothermic machine perfusion (HMP) is an established clinical benchmark, particularly for higher-risk deceased-donor kidneys. In a 2024 meta-analysis pooling 3,109 participants from 16 HMP-versus-SCS studies, HMP reduced the risk of delayed graft function by 23% relative to static cold storage (RR 0.77, 95% CI 0.69-0.86).[5] This estimate concerns delayed graft function and should not be interpreted as evidence of improved long-term graft survival. Dynamic perfusion also offers capabilities that static storage cannot: continuous physiological monitoring, viability assessment, oxygen delivery, and potentially targeted repair. The most useful future pathway may therefore be sequential. A kidney could be stabilized for transport by supercooling, then rewarmed and placed on a perfusion circuit for functional testing or intervention before implantation. Such a sequence would combine the logistical reach of storage with the biological information, resuscitation, and intervention enabled by perfusion.

Enthusiasm must nevertheless be proportional to the maturity of the evidence. The larger series reported in the news has not yet been presented with transparent group sizes, prespecified endpoints, variance estimates, or complete adverse-event reporting. The news report and conference abstract arise from the same broader research programme and should not be counted as independent replications.[1,2] The separate peer-reviewed 24-48-h study provides important context but does not independently validate the headline 72-h series.[3] A successful transplant demonstrates feasibility, but it cannot establish reliability, noninferiority, or superiority. In a preservation technology, rare catastrophic failures may matter as much as average graft function.

The animal model also leaves clinically important questions open. Autotransplantation avoids alloimmune injury and does not reproduce the immunological uncertainty of deceased-donor transplantation. Young healthy porcine kidneys may tolerate cold and rewarming differently from older human kidneys, donation-after-circulatory-death grafts, or organs with vascular disease and acute injury. Delaying removal of the contralateral kidney for several days provides a pragmatic postoperative safety bridge, but it also means that the preserved graft is not the sole source of renal function during the earliest and most vulnerable period. Future studies should include immediate nephrectomy models where ethically and technically justified, allotransplantation, marginal-donor phenotypes, and blinded histopathology extending well beyond 30 days.

Engineering validation will be equally decisive. Supercooling is metastable: contamination, microscopic gas pockets, surface defects, vibration, and temperature gradients can trigger ice nucleation. Scaling from a controlled laboratory chamber to routine procurement introduces motion, air transport, repeated handling, power interruptions, and variable ambient conditions. Each device will need redundant temperature and phase-change sensors, fail-safe power, continuous data logging, validated alarm and action thresholds, and preset quarantine or discard rules after a suspected excursion. Transport qualification should define orientation, vibration, pressure, and ambient tolerances as well as post-transport graft-release criteria. The system must also demonstrate uniform cooling and rewarming throughout the cortex, medulla, vasculature, and ureter. Calibration, self-test performance, battery reserve, and the chain of custody for device logs should be verified before every use. Release decisions should be auditable rather than dependent on unrecorded operator judgment. A device that extends average storage time but occasionally produces undetected local freezing would be clinically unacceptable.

In the United States, regulatory planning should begin with early FDA dialogue to clarify device classification, nonclinical testing, and the appropriate investigational-device pathway. Pre-submission discussion should align

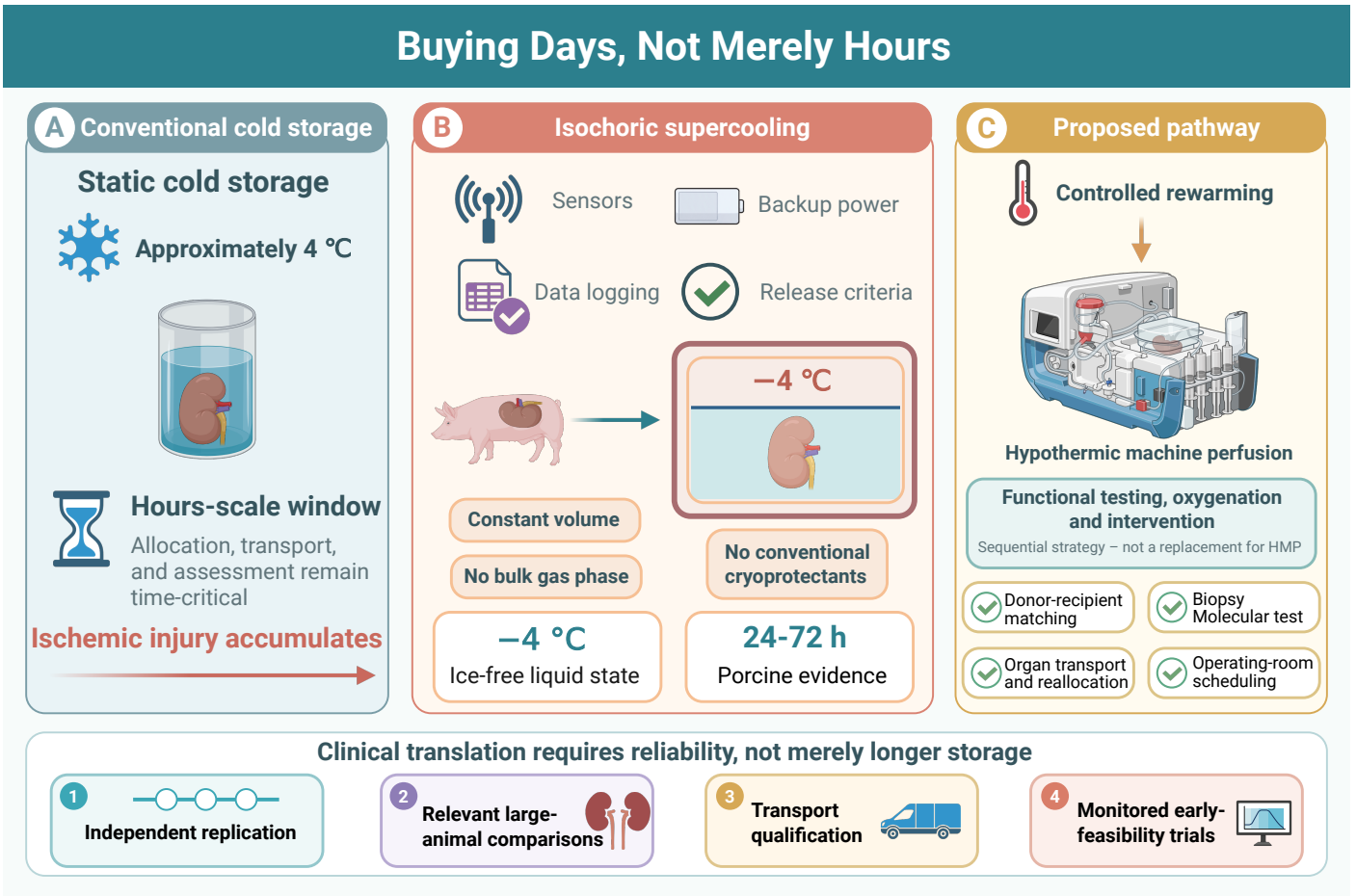

Figure 1. Isochoric supercooling for kidney preservation: potential and translational requirements (A) Static cold storage slows metabolism, but ischemic injury accumulates and limits the time available for transplantation. (B) Isochoric supercooling maintains an ice-free liquid state at −4 °C under constant-volume conditions, with reported porcine preservation durations of 24–72 h. (C) A proposed pathway links supercooling to HMP for graft assessment and potential intervention, allowing more time for donor–recipient matching, transport, and surgical scheduling. Clinical translation requires replication, large-animal comparisons, transport validation, and monitored early-feasibility trials. HMP, hypothermic machine perfusion.

design verification, transport qualification, human-factors testing, and risk controls with the proposed clinical use. Breakthrough Device designation could be considered only if statutory eligibility criteria are met; it is a voluntary mechanism for prioritized interaction, not a substitute for evidence of safety and effectiveness. Any first-in-human study would also require the applicable regulatory authorization, institutional review, and robust device accountability.

The next experiments should therefore be designed as a translational program rather than a sequence of record-setting storage durations. First, independent laboratories should reproduce the 24-, 48-, and 72-h results using standardized protocols and predefined functional and histological endpoints. Second, powered large-animal studies should compare isochoric supercooling with both contemporary static cold storage and hypothermic machine perfusion, including donation-after-circulatory-death and extended-criteria donor kidneys. Third, transport qualification should stress-test vibration, orientation, pressure changes, and delayed recovery. Only after these steps should clinical evaluation proceed through a staged, small early-feasibility study focused first on device performance and safety. A sequential supercooling-to-HMP protocol with a concurrent standard-of-care comparator would be preferable to reliance on historical controls alone. Prespecified stopping rules should cover device failure, primary nonfunction, and serious graft-related complications, with independent data monitoring and transparent reporting of temperature excursions, ice formation, and device malfunctions. Delayed graft function, dialysis requirement, vascular and ureteric complications, rejection, kidney function, and 1-year graft survival should also be reported. Because a small early study would not be powered to establish effectiveness, these clinical outcomes should be prespecified as descriptive or exploratory, and enrollment should proceed in stages with independent review before expansion.

The real promise of isochoric supercooling is not that it freezes time, but that it may make transplantation less hostage to it. The porcine findings are best regarded as a landmark preclinical proof of concept; clinical landmark status will require independent replication, transport validation, and appropriately monitored human trials. If those tests are met, buying two additional days could prove more transformative than the temperature change itself.

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DECLARATION OF INTERESTS

The authors declare no competing interests.