Report N. 1

LIFTT TECHNOLOGY INSIGHTS

Engineering the human body: beyond tissue and organ scarcity

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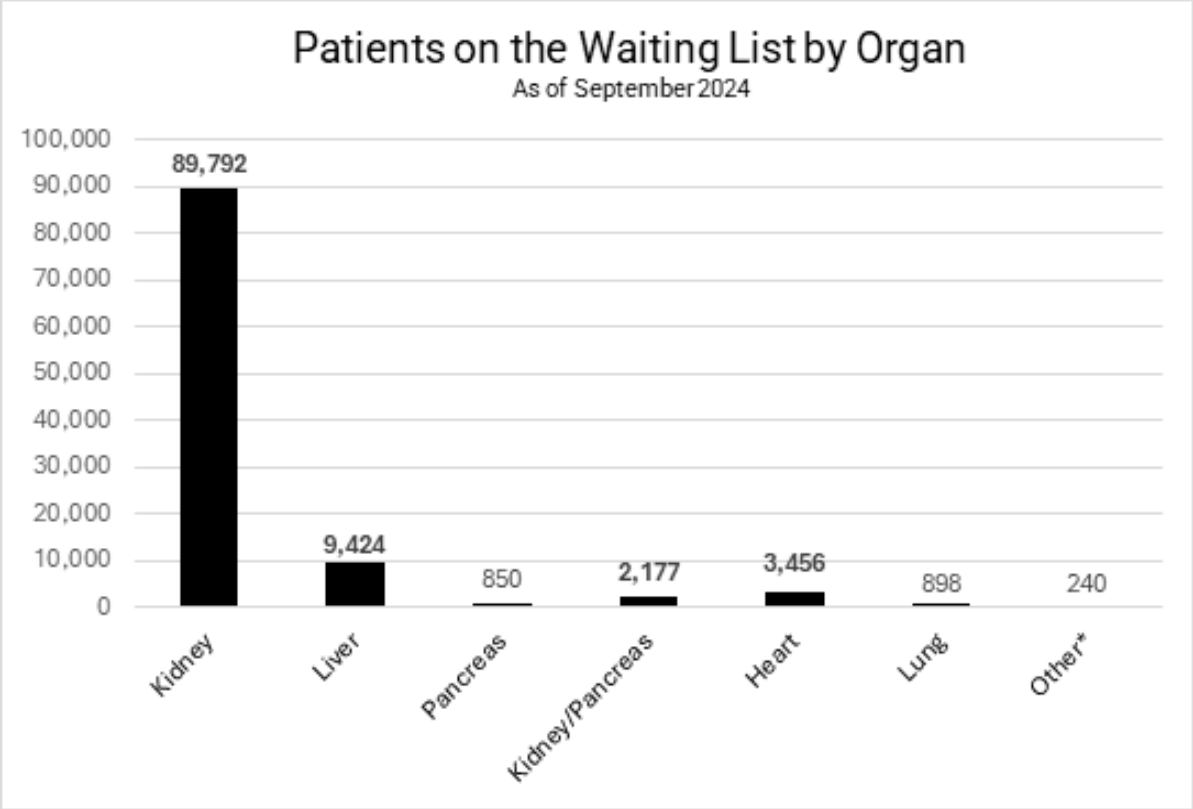
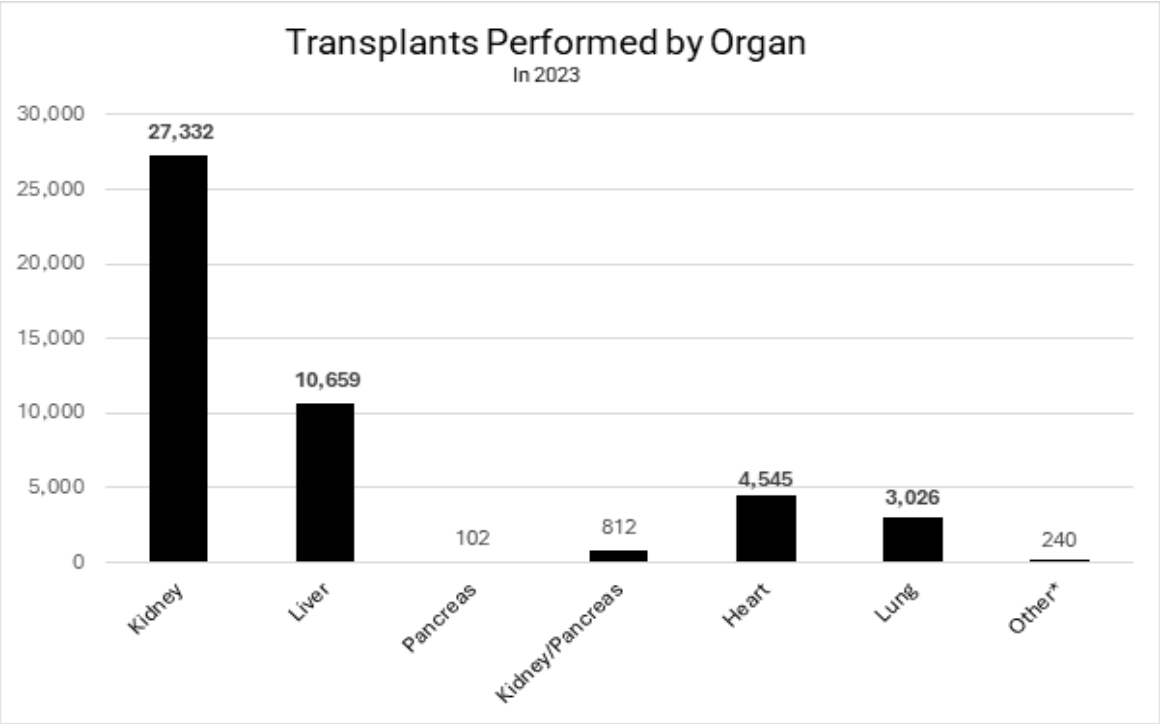
Tissue and organ engineering and preservation are converging to respond to growing clinical demand: long waiting lists, organs and tissues that deteriorate before implantation, avoidable waste. The model based solely on donors and traditional ice preservation is no longer able to cope with the timescales, volumes, and clinical variability involved.

In this context, the engineering and preservation of tissues and organs is an innovation with very strong demand pull: to date, over 100,000 patients in the United States are waiting for a life-saving transplant, and about 17 of them will die today without finding an available organ. In Europe, the situation is no better. In 2022, ~48,000 new patients were placed on waiting lists and ~7,300 died while on the list (≈19 per day).The comparison below between snapshots of waiting lists and annual transplant flows highlights a persistent mismatch in the US: what accumulates on the list at a given moment is not absorbed by the annual pace of procedures.





*Other includes allograft transplants like face, hands, and abdominal wall.
Based on OPIN data as of September 15, 2024. Data subject to change based on future data submission or correction. Totals may be less that the sums due to patients included in multiple categories.

US data organdonor.gov - The graph "Patients on the Waiting List by Organ in September 2024" represents a snapshot of a specific day (September 15, 2024), showing how many patients were on the waiting list at that point in time. In contrast, "Transplants Performed by Organ" illustrates the total number of transplants carried out over a longer period (in this case, across the whole of 2023), rather than on a single day. It is important to note that waiting lists change daily, as patients are continually added and removed. These graphs therefore provide only high-level insights into transplant activity: the first offers a point-in-time picture, while the second reflects annual activity. They are not directly comparable, and in some categories the same patient may be counted more than once. Instead, they should be read as indicative of the scale of the gap between demand and the system's current capacity.

To bridge this gap between supply and demand, three technological strands are under development and have the potential to change the rules of the game:

- Advanced preservation: from ex-vivo normothermic perfusion to the first subzero platforms to extend the useful window and recover 'marginal' organs.
- Xenotransplantation with genetic editing: CRISPR and multi-editing to increase the supply of compatible organs.
- Biomanufacturing: bioprinting, scaffolds, and cells to create on-demand tissues and increasingly functional grafts.

It is a clinical emergency that requires us to move beyond the classic donor-based model, which is no longer able to meet the real needs for tissues and organs.

DEEP SIGNALS

In recent years, a concrete transformation towards an 'on-demand' model for tissues and organs has been set in motion. Among the three technological directions that are helping to accelerate the transition from theory to practice, there are concrete signs of progress.

1. Preservation of tissues and organs

Transplant logistics are undergoing a transformation. Cold storage in ischemia is being complemented (and in some cases replaced) by ex-vivo perfusion systems at normal temperature, which have already arrived in clinics: the organ is no longer "kept on ice," but connected to a machine that circulates oxygenated solutions at body temperature, keeping it alive and functioning until transplantation (Transmedics, a leader in normothermic perfusion, reports that 3,715 procedures were completed in the United States in 2024, an increase of 58% compared to 2,347 in 2023). At the same time, new cryopreservation and subzero storage strategies aim to extend time windows and expand transport ranges. For example, X-Therma reports significant results: transatlantic transfers of pig kidneys in approximately 48 hours, maintaining conditions compatible with transplantation and using commercial flights. If these approaches become standardised, the geography and timing of donation will change: more possible matches, fewer discarded organs, greater equity of access.

2. Genetic editing and xenotransplantation

Alongside improvements in logistics, there are more 'cutting-edge' developments: xenotransplantation and genetic editing (CRISPR) to adapt animal organs and reduce immunogenicity in human patients. Clinical feasibility was demonstrated in January 2022 with the first pig-to-human heart transplant: patient David Bennett lived for several weeks thanks to a pig heart with 10 genetic modifications. Although not a lasting success, this case opened up a regulatory and scientific breakthrough. Along the same lines, United Therapeutics announced the advancement of the UKidney program toward clinical trials following FDA approval. Even more recent is the attempt to xenotransplant a pig lung into a clinically dead man at The First Affiliated Hospital of Guangzhou Medical University in China, which recorded nine days of vital activity. It remains a complex field (rejection, immunological management, zoonotic risks), and many of the patients who underwent xenotransplantation died relatively soon after the operation, but there are signs that the learning curve is accelerating.

3. Engineered tissues and biomanufacturing

3D bioprinting, scaffolds, and cell engineering are moving from iconic demonstrations to platforms. In 2022, 3DBio Therapeutics performed the first transplant of a 3D-printed ear from autologous cartilage cells. On the vascularization front, Symvess received FDA approval in December 2024 for its acellular engineered blood vessel developed by Humacyte, designed for use in urgent revascularization cases. Although this remains the real bottleneck for complex organs, research has made important strides: from Tel Aviv University (3D mini-heart with chambers and main vessels) to techniques developed at Harvard/Wyss for intricate vascular networks with smooth muscle and endothelial cells lining a functional hollow lumen. The goal is to replicate the architecture and function of natural vessels within thickened tissues, an essential requirement for scaling up to the liver, kidney, and lung.

4. Priority regulatory pathway and public market

On the regulatory front, there are signs of openness: the FDA has already granted Breakthrough Designation and accelerated pathways such as Regenerative Medicine Advanced Therapy (RMAT) to pioneering products. Emblematic cases include X-Therma, with its cryopreservation platforms, BMI OrganBank, and Symvess, which also obtained FDA approval in 2024. At the same time, TransMedics' steady growth on the stock market — resilient even to attempts by short sellers — confirms that the market rewards companies capable of responding to clinical gaps with concrete and scalable solutions.

WHAT DO THESE SIGNS TELL US?

They tell us that an integrated value chain is taking shape: preservation (normothermia/cryobiology) to gain time and clinical quality; xenotransplantation/editing to expand the offering; biomanufacturing to move closer to personalized tissues and, in the future, organs. At the same time, the regulatory front is showing openings (Breakthrough, RMAT) that clarify the scope of authorization; the public market confirms the attractiveness of the issue. The trajectory points to a more scalable model, in which structural scarcity is no longer a fate but an engineering problem to be solved.

WHAT'S GOING ON IN THE MARKET?

The movement is real on several fronts. In bioproduction, the 3D printing giants stand out among the technological incumbents: 3D Systems has built a dedicated presence in regenerative medicine, including through targeted acquisitions, such as the integration of Volumetric Biotechnologies (co-founded by Jordan Miller), with the stated goal of bringing organ bio-manufacturing to industrial scale-up.
On the biotech-pharmaceutical side, players such as United Therapeutics are putting together integrated portfolios covering xenotransplantation, bioartificial organs, and perfusion platforms. Corporate/VC interest is also growing in preservation devices: in 2025, OrganOx closed a round with the entry of Intuitive Ventures (Intuitive Surgical) and Terumo Ventures and also received a purchase offer from Terumo itself, a sign of the growing strategic attention of those who already oversee the operating room and the cardiovascular supply chain.

On the startup side, the landscape is dense and global. In biofabrication, in addition to the aforementioned Volumetric, there are 3DBio Therapeutics (USA), BICO/Cellink (Sweden), Aspect Biosystem, Organovo, Cyfuso, FluidForm, and younger companies such as Cellbricks (Germany), focused on different levels from scaffolds to bioinks to bioprinters. In xenotransplantation, in addition to eGenesis, Qihan Biotech (China) and Makana/Revivicor (USA) are active with engineered pig lines and initial clinical protocols in collaboration with centers of excellence.

In organ preservation and perfusion, TransMedics has industrialized the Organ Care System (OCS) to maintain the heart, lungs, and liver in near-physiological conditions during transport. OCS (Organ Care System) is an FDA-approved device for use on standard and extended criteria, enabling new transplant capabilities. Alongside TransMedics, XVIVO Perfusion and OrganOx are respectively dominating expanding markets and indications with perfusion solutions for different organs.

Paragonix Technologies joins the cold chain, expanding its family of temperature-controlled transport systems designed to standardize storage variables and monitor temperature trends in real time. The device has obtained 510(k) clearance and is intended to support more predictable logistics for pancreas transplants as well. In the field of cryopreservation, X-Therma is making a name for itself with its product line, including XT-Vivo, which could revolutionize the logistics of organ and tissue transport by guaranteeing a shelf life that was unimaginable until now.

Startups such as Vivalyx and BMI OrganBank are also emerging, working on liquid solutions for blood-free perfusion to improve ex-vivo organ management. The innovation system is also fueled by leading academic hubs — from Anthony Atala's Wake Forest Institute to MIT/Harvard, ETH Zurich, and the Institut Pasteur — which are the source of many of the platforms currently being spun off.

Concrete examples confirm the ongoing consolidation: in 2025, Terumo acquired OrganOx (≈$1.5 billion), strengthening its liver perfusion capabilities; in 2024, Getinge completed the acquisition of Paragonix (up to $477 million) for temperature-controlled transport systems; in 2023, United Therapeutics acquired Miromatrix ($91 million) to integrate bioengineered organs; in 2021, 3D Systems bought Volumetric (up to $400 million), pushing bioprinting towards scale-up; on the capital markets front, TransMedics debuted on NASDAQ (2019, ~$91 million) and Humacyte went public via SPAC (2021), signaling stable access to "patient" capital.

The first exits and stock market listings indicate a dual pattern: vertical integration (from preservation to logistics to "organ manufacturing") and technological convergence (device + bio + supply chain). The moves on OrganOx and Paragonix show how large medtech companies are dominating transport and storage; operations such as Miromatrix and Volumetric are accelerating organ manufacturing from PoC to clinical-industrial scalability; the stock market (TransMedics, Humacyte) provides regulatory visibility and long-term capital. At the same time, workflows from cold storage to dynamic perfusion (hypothermic/normothermic) are converging on shared procedures and standards, reducing variability between centers. In other words, the transplant system is moving from random scarcity to a more programmable infrastructure, with expected impacts on clinical outcomes, costs, and access.

TECHNOLOGICAL AND MARKET CHALLENGES

There is strong enthusiasm, yet significant obstacles persist: the revolution in engineered tissues and organs faces biological complexities, long lead times, and regulatory frameworks are still being developed.

Scale and biological complexity

Creating a functioning human organ is anything but straightforward. Biomanufacturing faces the challenge of vascularization: replicating the microarchitecture of a kidney or lung means reconstructing millions of perfectly integrated microscopic structures. This requires biomimetic bio-inks, intelligent scaffolds, and cell production systems capable of generating billions of autologous cells in clinical timeframes. Even when the anatomy is replicated, the issue of functionality remains: a tissue must integrate and function like the original, not just resemble it. On the xenotransplantation front, multiple genetic edits are still not enough to defuse the complexity of the human immune system, which can generate subacute rejection or unexpected inflammatory reactions. Some groups, such as Revivicor, are experimenting with complementary solutions — such as inserting the donor's thymus — to promote immunological tolerance. In cryopreservation, the transition from small organs (a mouse kidney measuring a few centimeters) to human organs such as the liver (~1.5 kg) remains critical: the diffusion of cryoprotectants, thermo-mechanical stresses, and post-thaw reperfusion are issues that have not yet been resolved.

Development times and hype risk

Advances are tangible – first pig hearts transplanted, printed tissues, organs perfused for days – but widespread clinical adoption remains a long way off. Experts estimate that complete 3D-printed organs will not be available for 15-20 years, and even for xenotransplantation, the realistic goal is towards the end of this decade.

This gap risks fueling a misalignment between clinical expectations and technological timelines, but also between capital investment cycles and the scientific horizon. If not managed transparently, hype can erode trust: early successes must be presented as intermediate steps, not definitive solutions.

Regulation and safety

Regulatory frameworks are still being defined. Is a bioprinted organ a medical device, an ATMP, or something new? The answer will determine the authorization paths and GMP standards required. In xenotransplantation, in addition to rejection, the issue is zoonotic risk: even if the new pig lines are free of endogenous retroviruses (PERVs), authorities will likely require special registries and long-term monitoring protocols. Bio-manufacturing, on the other hand, faces standardization challenges: how can we ensure that a liver produced in a laboratory in Boston is identical to one made in Zurich? Advanced quality control tools, such as organ-on-chip models or digital simulations, will be needed to reduce variability and gain regulatory confidence.

Summary

The bottlenecks are scientific, industrial, and social. There are no shortcuts, but clearly identifying the risks paves the way for solutions: investing in targeted research (vascularization, immunology, GMP standards), building early and flexible regulatory frameworks, engaging society in a transparent debate, and maintaining an ethics-centric approach. Only then can the extraordinary potential of tissue and organ engineering and preservation be transformed into real and lasting clinical benefits.

WHAT TO EXPECT NOW

The clinical urgency is becoming more evident every day, and with it, the economic pressure: the current transplant system is expensive, inefficient, and unable to meet growing demand. This is generating an unprecedented demand-pull push towards innovative solutions. Over the next 12-24 months, we will see the launch of numerous clinical trials across different technological strands. The initial data will not only guide scientific trajectories, but will also serve as a guide for regulators, outlining clearer authorization paths. At the same time, renewed interest from venture capital is expected, ready to channel resources already in the preliminary phase now that the technological and regulatory roadmap appears less uncertain.
The sector seems to have moved beyond the basic scientific de-risking phase: today, it is ready to tackle more specific challenges that require vertical solutions, robust enabling technologies, and, above all, the ability to integrate different trajectories into a convergent ecosystem. It is at this stage that industrial vision — rather than individual discoveries — will make the difference.

DEEP IMPACT

If current progress continues, what outcomes can reasonably be expected? The emergence of on-demand tissues and organs, transplants without waiting lists, and cryopreserved organ and tissue banks would constitute a transformative development in the treatment of related diseases, with the potential to profoundly reshape global healthcare systems. Yet, as has been noted, the transition from the laboratory bench to the patient's bedside requires considerable time, substantial financial investment, and the collaboration of multiple disciplines.

Should these technologies become established, the transplantation system would evolve from an emergency-driven model to one that is planned and programmable:

- Supply chains: the development of organ biobanks and global temperature-controlled logistics, supported by the convergence of devices, biology, and artificial intelligence.
- Policy: the creation of harmonized standards for safety and quality, equitable access, and robust traceability mechanisms.
- Clinical practice: reductions in rejection rates and mortality, predictable surgical schedules, and greater consistency in outcomes.
- Hospital economics: lower costs due to fewer complications and shorter hospital stays, along with reduced pressure on dialysis and other bridge therapies.

In conclusion, this evolution signals a transition from chronic scarcity to an on-demand infrastructure for tissues and organs — an ecosystem in which biological design, logistics, and regulatory frameworks work in concert to bring care directly to the patient, rather than requiring the patient to seek care.

Sources

- Official sources / Institutional data:
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- Scientific literature (peer-reviewed):
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- Corporate websites and Investor Relations:
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