Engineering whole organs: Closing in on a potential solution to the organ donor shortage?

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A new technique involving the use of an artificial scaffold into which a patient's own stem cells are inserted, turning it into a fully functional organ, could offer a potential solution to the donor shortage crisis, according to the second paper in this week's *Lancet* Series on stem cells. This pioneering approach to regenerating and transplanting organs requires no human donors, has no problems with rejection, and has no need for immunosuppressive drugs.

"Such an approach has already been used successfully for the repair and reconstruction of several complex tissues such as the trachea, oesophagus, and skeletal muscle in animal models and human beings, and guided by appropriate scientific and ethical oversight, could serve as a platform for the engineering of whole organs and other tissues, and might become a viable and practical future therapeutic approach to meet demand after organ failure", explains Paolo Macchiarini from the Karolinska Institutet, Stockholm, Sweden, lead author of the paper.

Because of an ageing population there is a growing crisis in whole-organ donor supply. Every year in the USA alone, about 120 000 people die from chronic lung disease, 112 000 from kidney failure, and 425 000 from coronary heart disease. Patients who are fortunate enough to receive a donor organ still face life-long expensive and potentially dangerous immunosuppressive therapy.

In this paper, Macchiarini and colleagues discuss the use of a new regenerative technique based on the use of naturally occurring extracellular matrix as a biological scaffold, outline the key scientific and ethical challenges that remain before wider clinical use of this approach is possible, and review progress made in the reconstruction of individual organs.

Identification of the optimum cell sources for different organs, the ideal scaffold material, and the appropriate population of patients are some of the key challenges that will need to be addressed before widespread clinical use.

"For clinical trials, due consideration needs to be given to who to recruit: suitable patients should be able to provide competent consent, have some amount of social support, have few comorbidities, and be willing to face loss of privacy", say the authors.

As well as scientific challenges, more needs to be done to address the numerous ethical issues raised by this new technology. "The pressure to advance this technique, driven by demand, the race for prestige, and the potential for huge profits, mandates an early commitment be made to establish the safety of various strategies…particularly when there are so many potential patients and doctors who are desperate for any remedy that offers hope", warn Macchiarini and colleagues.

They conclude by calling for policies to address issues including: transparency about the techniques involved, cell sources, financial costs to patients, informed consent, strategies for dealing with experimental failure, and assisting patients after initial treatment, adding that: "Perhaps the strongest ethical duty the bioengineering community faces is the identification of criteria that constitute sufficient evidence of the evolution of an intervention from research to therapy…Establishment of adequate safety and functional success will need input from investigators

and key professional societies and organisations."

In an accompanying Comment, Dusko Ilic from King's College London, UK, and Julia Polak from Imperial College, London remark: "Although several questions are unresolved, the promise of an off-the-shelf scaffold that can be repopulated with autologous stem cells expanded in vitro seems much closer than one could have hoped for even a few years ago."

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