EDITORIAL

Regional Organ Assessment and Repair Centers (ARCs)

Sylvester M. Black[1,2] and Bryan A. Whitson[1]

The Collaboration for Organ Perfusion, Protection, Engineering and Regeneration (COPPER) Laboratory of The Ohio State University Wexner Medical Center[1]
The Ohio State University Department of Surgery Divisions of Transplantation[2] and Cardiac Surgery[3]

Corresponding author: Dr. Bryan A. Whitson Email: bryan.whitson@osumc
Published: 11 September 2013
Ibnosina J Med BS 2013;5(5):243-246
Received: 20 August 2013
Accepted: 23 August 2013
This article is available from: http://www.ijmbs.org

Organ transplantation by any measure is one of the success stories of modern medicine. The multidisciplinary approach, the complexity of disease, the scientific innovation and the truly excellent outcomes associated with modern transplantation give hope to both patients and clinicians worldwide. The field of transplantation, like many others proceeded along in a stepwise fashion, with small incremental improvements in technology and scientific understanding, giving way to significant breakthroughs in our understanding of the immune system and the pathophysiology of end stage organ disease. Conceptually organ transplantation has an ancient past, with accounts of saints, healers, and Gods performing transplantation of limbs and organs between individuals. In the 1930's the French-American surgeon-scientist Alexis Carrel carried out a series of important experiments that were breathtaking in their scope and impact, in which various organs such as the kidney, heart, thyroid, and limbs of animals were transplanted (1). These transplants functioned for a period of time and demonstrated the technical feasibility of transplantation in general and vascular anastomotic technique in particular (2). Carrel would go on to perform many transplants between animals and within the same animal. Without exception organs would function indefinitely as auto-transplants but when transplanted into different animals would cease to function after a short period of time.

Carrel correctly recognized the concept of rejection and commented about biological "individuality" as a barrier that could not be crossed by surgical means.[2] Carrel understood the innate difficulties associated with transplantation that would later be borne out by others with further experimentation and clinical trial. While Alexis Carrel is well known for organ transplantation and vascular anastomosis for which he was awarded the Nobel Prize in 1912, it is some of his other work that currently has the most profound implications for the field of transplantation.

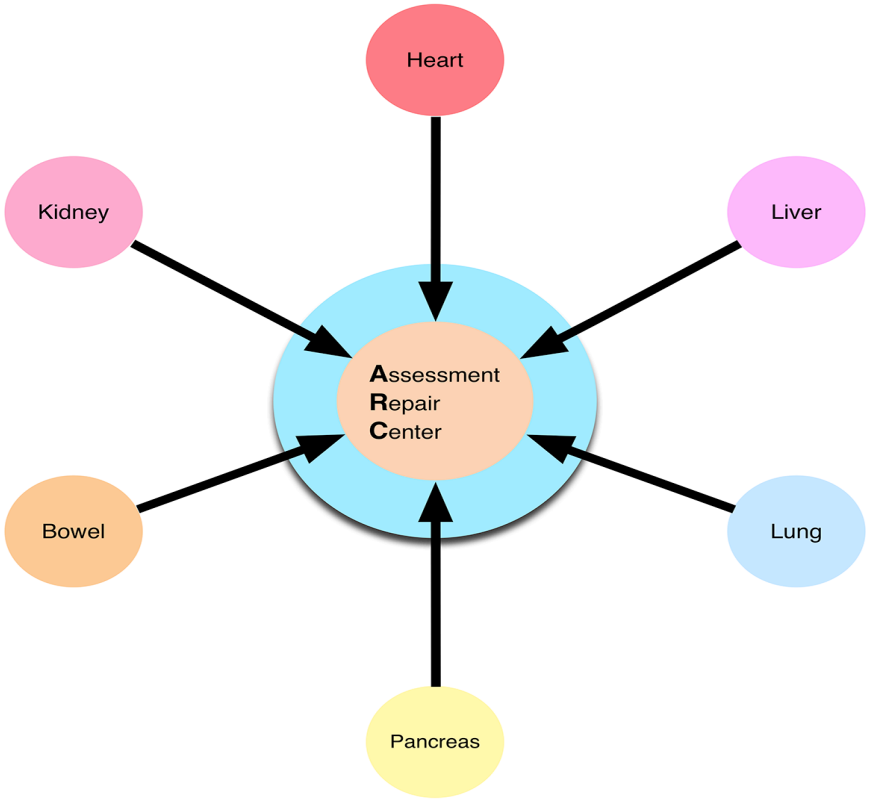

Figure 1 a. Organ ARC's (Assessment and Repair Centers) would take in donor organs regionally, for assessment. Decisions about the quality and viability of the organs would be made at that time. ARCs may have specializations in various organ types such as lung, and heart or may be more general.

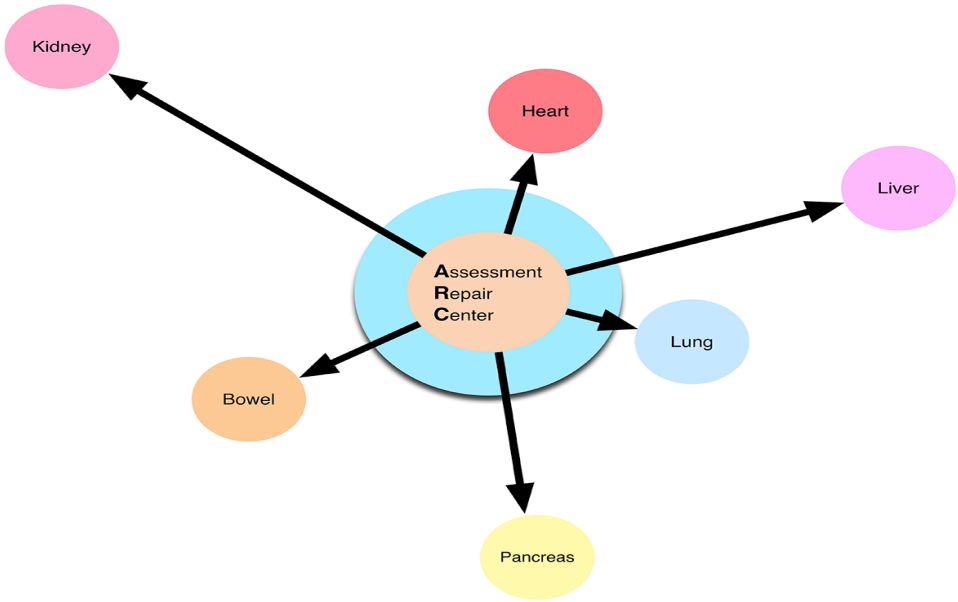

Figure 1 b. Organs that are deemed to be of sufficient quality after assessment or after repair would be sent to the appropriate recipient.

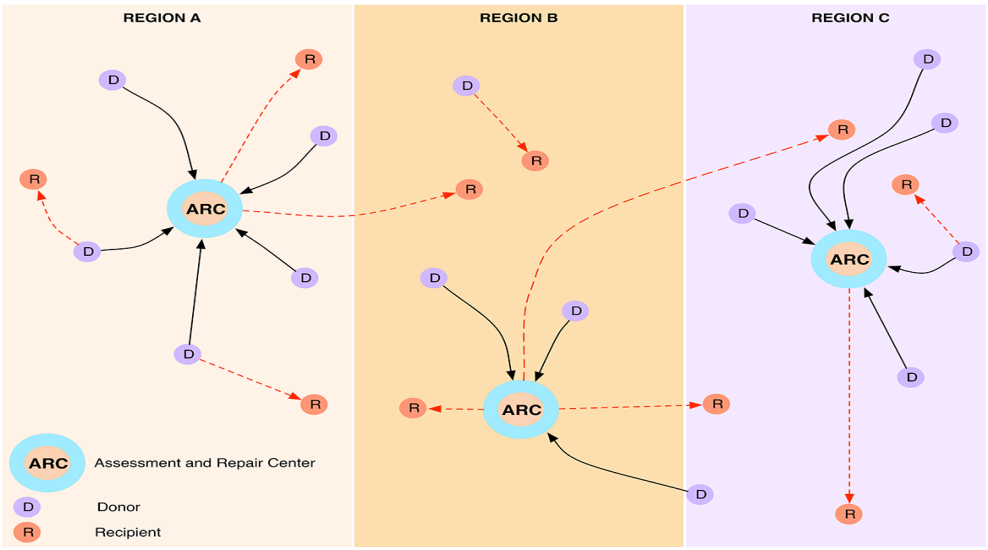

Figure 1 C. With EVOP (ex-vivo organ perfusion), greatly extended preservation times would allow for organs to travel great distances and regions to the appropriate recipients. In some instances it may be more appropriate to perform the more traditional approach and transplant the donor organs directly into the recipient bypassing the ARC (Assessment and Repair Centers).

Carrel was responsible for developing the technique of cell and tissue culture, which is a widely practiced technique in modern research. Carrel with the aid of the aviator Charles Lindbergh also developed a perfusion apparatus in which he was able to keep whole organs such as the thyroid gland alive in conditions that approximated normal physiology for weeks at a time (3,4). These were the first "ex-vivo normothermic" perfusion experiments and are very much the progenitors of modern methods. Carrel essentially saw people as collection of parts that could be supported, repaired and regenerated outside the body in these perfusion systems. When an organ became diseased or injured it could simply be replaced with another functional one from the laboratory. In a way, they very much saw this as a method to extend life indefinitely.

The progress of organ transplantation unfortunately would not be that smooth. The cumbersome nature of these perfusion systems, the reliability, cost, along with a host of other technical factors caused the abandonment of these normothermic perfusion systems in favor of simple cold storage and speedy implantation. Transplant pioneers Najarian and Belzer attempted to overcome ischemia and reperfusion injury by swift implantation of kidneys, often starting the recipient operation before the donor operation was complete. With these techniques there was improvement in organ function post transplantation (5). The concept of cold storage, with lowering of the organ's metabolic rate combined with better preservation solutions such as University of Wisconsin solution further improved organ survival. Extended preservation was then achieved by Belzer utilizing hypothermic machine preservation to achieve a total preservation of 37 hours for a kidney that was implanted in the Netherlands. The ability to achieve prolonged preservation time with machine hypothermic perfusion systems in metabolically active organs such as the liver and heart was not met with the same success and generally abandoned during this time period.

Simple cold storage and hypothermic machine preservation, while appreciably lowering the metabolic rate and increasing preservation times do not allow for optimal assessment of an individual organ. Most of the determinations regarding an organ's function are made pre-procurement and while hypothermia decreases the metabolic rate of the donor organ, significant anaerobic metabolism continues to take place. Prolonged preservation and marginal donor organ quality can lead to significant delayed graft function or graft non-function in the recipient.

These factors have lead to a renewed interest in normothermic perfusion of donor organs. With improvements in miniaturization, computing, knowledge of organ physiology, development of new normothermic perfusates and pump technology, the concept of real time organ assessment with the possibility of intervention to

improve organ quality has become a reality.

The potential of ex-vivo organ perfusion for the assessment and improvement in donor organ quality is illustrated by the work of Wigfield and colleagues where a marginal set of donor lungs were transported internationally from the United States to an organ repair center at the University of Toronto. The lungs were assessed, reconditioned and transported back to the United States for transplantation. The total time the organs were outside of the donor was 15 hours and 20 minutes (6). Currently there is a multi-institutional trial in the United States to evaluate ex-vivo lung perfusion and in Canada it is used clinically at the University of Toronto. Ex-vivo lung perfusion has demonstrated the ability to reduce or remove edema, clear infection and improve gas exchange (7).

Recent successes in ex-vivo liver perfusion were also demonstrated in the United Kingdom at King's College Hospital where a liver was normothermically perfused on a circuit prior to transplantation (8). Ex-vivo organ perfusion (EVOP) has also demonstrated the ability in the laboratory to mitigate bile duct injury (9), reverse steatosis (10), and limit ischemia-reperfusion injury improving overall organ quality and function. Currently there is a European trial to investigate the clinical use of ex-vivo liver perfusion technology.

These clinical and laboratory successes demonstrate that normothermic EVOP can serve as a viable platform for accurate organ assessment and repair. A significant consequence of the success of normothermic EVOP is the concept of a regional organ Assessment and Repair Centers (ARC). Regional centers would have the ability to assess and make the necessary interventions to optimize donor organ quality and function (figure 1 a, b, c). With these improvements as well as greatly extended preservation times it becomes possible to more precisely match donor and recipient, improve donor organ quality and thus improve transplantation outcomes.

References

1. Carrel A. Landmark article, Nov 14, 1908: Results of the transplantation of blood vessels, organs and limbs. By Alexis Carrel. JAMA. 1983;250:944-53.
2. Schlich T. The origins of organ transplantation. Lancet 2011;378:1372-3.
3. Carrel A. The Culture of Whole Organs : I. Technique of the Culture of the thyroid gland. The Journal of experimental medicine 1937;65:515-26.
4. Carrel A, Lindbergh CA. The Culture of whole organs. Science 1935;81:621-3.
5. Belzer FO. Organ preservation: A personal perspective. In: Terasaki PI, ed. History of Transplantation: Thirty-five Recollections: UCLA Tissue Typing Laboratory. 1991:595-614.
6. Wigfield CH, Cypel M, Yeung J, et al. Successful emergent lung transplantation after remote ex vivo perfusion optimization and transportation of donor lungs. Am J Transpt. 2012;12:2838-44.
7. Cypel M, Yeung JC, Liu M, et al. Normothermic ex vivo lung perfusion in clinical lung transplantation. N Engl J Med. 2011;364:1431-40.
8. Foley JA. New technique keeps liver 'alive' outside the body then transplanted to new patient, may increase number of successful liver transplants. Nature World News 2013. [cited 2013 August 19]; available from: http://www.natureworldnews.com/.
9. Boehnert MU, Yeung JC, Bazerbachi F, Knaak JM, Selzner N, McGilvray ID, et al. Normothermic acellular ex vivo liver perfusion reduces liver and bile duct injury of pig livers retrieved after cardiac death. Am J Transplant. 2013;13:1441-9.
10. Nativ NI, Maguire TJ, Yarmush G, et al. Liver defatting: an alternative approach to enable steatotic liver transplantation. Am j Transp. 2012;12:3176-83.