



Why do we need tissue engineering?

Reconstructive plastic surgery integrates the art and science of restoring the functional and aesthetic properties of defective or lost tissue. Current methods for reconstruction include the transfer of uninjured tissue harvested from the patients themselves or from live or cadaveric donors. Although the use of various grafts and flaps is widespread, such techniques are limited by a lack of available donor tissue, donor site morbidity and complicated surgery. The use of non-biological implants is also an imperfect solution associated with its own set of complications.

The rapidly evolving field of tissue engineering is being increasingly applied to the practice of plastic surgery and presents an innovative approach to tissue replacement, avoiding the complications associated with traditional reconstructive techniques.

History and development

The term 'tissue engineering' was first introduced at the Washington National Science Foundation meeting in 1987 and has since been defined as "an interdisciplinary field that applies the principles of engineering and life sciences toward the development of biological substitutes that restore, maintain or improve tissue or organ function." (1) The modern era of tissue engineering is said to have emerged in the 1980s, with the development of engineered skin substitutes (2). However, it was only in 1997, following a BBC broadcast on the potential of tissue-engineered cartilage, that the technology gained public awareness. One of the images shown was the infamous 'mouse with the human ear' (Fig. 1.)



Fig. 1. 'Mouse with the human ear' (3) - this image sparked controversy amongst animal rights activists as it was wrongly assumed to depict a genetically engineered mouse. In actual fact a polymer mold of a human ear had been seeded with bovine chondrocytes and implanted in the mouse's back.

In 1991, a 12 year-old boy born with Poland's syndrome (and absence of the sternum) became the first human to receive a tissue-engineered implant. It consisted of autologous chondrocytes grown on a synthetic polymer moulded into the shape of his chest (4). Recent research on stem cells and their ability to differentiate into various lineages has been of utmost importance in the application of tissue-engineering to clinical practice. In November 2008, Macchiarelli et al. reported the first ever trachea transplant using a patient's own adult stem cells (5). Today, researchers around the world are in the process of engineering biological substitutes for a variety of organs and tissues.

Basic principles of tissue engineering

Although three different approaches to tissue engineering have evolved (1) the most widely used method involves the following components: (i) cells (ii) a matrix or scaffold and (iii) signalling molecules. Successful tissue formation occurs when these components are placed in an appropriate environment and implanted into the host.

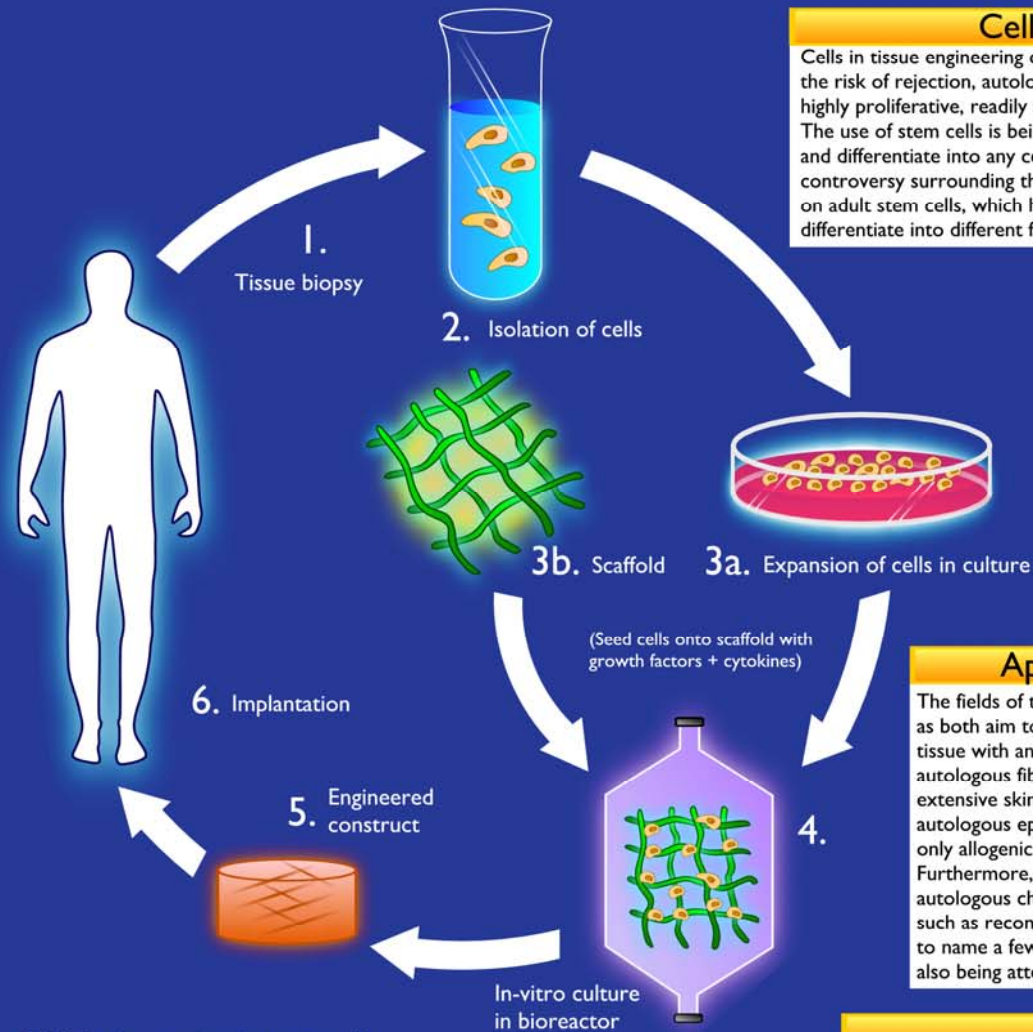


Fig 2. The tissue engineering process. (6)

1. A donor source for the cells is identified and a tissue biopsy is taken.
2. The desired cells are identified and isolated. They can be tissue specific, differentiated or progenitor cells, adult or embryonic cells.
- 3a. The cells are expanded in vitro to produce a viable population.
- 3b. Expanded cells are embedded onto a scaffold along with specific regulatory cytokines.
4. The cell/matrix is placed in a bioreactor, which may be designed to reproduce specific physiological conditions (i.e. pH, temperature, nutrients) to optimise cell and tissue growth.
5. Cell multiplication fills the scaffold with tissue and forms the desired structure.
6. The tissue construct is implanted into the host. The scaffold may dissolve whilst the cells further differentiate into functional tissue.

Cell sources and stem cells

Cells in tissue engineering can be autologous, allogeneic or xenogenic. Ideally, to limit the risk of rejection, autologous cells should be used. Furthermore, they should be highly proliferative, readily available and able to maintain a differentiated state in vivo. The use of stem cells is being actively researched due to their ability to self-renew and differentiate into any cell type from the three germ layers. Although there is controversy surrounding the use of embryonic stem cells, research is now focused on adult stem cells, which have no ethical concerns and have been shown to differentiate into different functional cell types and maintain a degree of plasticity (2).

Scaffolds/Matrices

Scaffolds provide a three dimensional matrix to facilitate cell growth. They can be produced from natural materials (e.g., collagen, hyaluronic acid) or synthetic polymers (e.g., polyglycolic acid, polylactic acid) (6). Ideal scaffolds should be biocompatible, bioabsorbable, nonimmunogenic and provide enough space for cell attachment and ECM deposition. Scaffolds are usually designed to biodegrade and gradually be replaced by the host's own tissue. Some scaffolds are now being embedded with growth factors that stimulate angiogenesis in the engineered tissue (6).

Applications in plastic surgery

The fields of tissue engineering and plastic surgery are closely related as both aim to fulfil the same purpose: to replace lost or damaged tissue with an aesthetic and functional living alternative. The culture of autologous fibroblasts and keratinocytes is being used in the repair of extensive skin wounds, such as burns and diabetic ulcers. Although autologous epidermal substitutes are commercially available, until now only allogenic dermal and bilayer products have been developed (7). Furthermore, engineering of cartilage is now possible using cultured autologous chondrocytes. This will have implications on procedures such as reconstructive rhinoplasty and nasal septal perforation, to name a few (7). The culture of autologous adipocyte precursors is also being attempted for those undergoing breast reconstruction (8).

Conclusion

Tissue engineering is closer than ever to revolutionising the way surgical reconstruction is carried out. Significant advances have been made in the past two decades due to the interdisciplinary cooperation amongst biologists, engineers, materials scientists and physicians. However, it is clear that further development and understanding of cellular mechanisms are needed if we are to expand the armamentarium of engineered tissue substitutes available to the reconstructive plastic surgeon.

References:
 1. Langer R, Vacanti J.P. Tissue engineering. Science. 1993; 260:920-926.
 2. Polak JM, Bishop AE. Stem cells and tissue engineering: past, present, and future. Ann N Y Acad Sci 2004 Apr;1048: pp. 352-366.
 3. Girl may be first to grow artificial ear. [Online] Available from: <http://news.bbc.co.uk/1/hi/sci/tech/77764.stm>.
 4. Vacanti CA. The history of tissue engineering. J Cell Mol Med 2006 Jul-Sep;10(3): pp. 569-576.
 5. Macchiarelli P, Jungbluth P, Go T, Arrighi PA, Ricci LE, Cogan JA, et al. Clinical transplantation of a tissue-engineered airway. Lancet 2008 Dec; 13(7219):655: pp. 2023-2030.
 6. Shieh SJ, Vacanti JP. State-of-the-art tissue engineering from tissue engineering to organ building. Surgery 2005 Jun;137(1): pp. 1-7.
 7. Patel NN, Butler PE, Buttery L, Polak JM, Tolley NS. Tissue engineering and ENT surgery. J Laryngol Otol 2002 Mar;116(3): pp. 165-169.
 8. Brey EM, Patrick CW Jr. Tissue engineering applied to reconstructive surgery. IEEE Eng Med Biol Mag 2000 Sep-Oct;19(5): pp. 122-125.