



## Historic Origins of the term Tissue Engineering

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### Description

Tissue engineering is a biomedical engineering discipline that uses a combination of cells, engineering, materials methods, and suitable biochemical and physicochemical factors to restore, maintain, improve, or replace different types of biological tissues. Tissue engineering often involves the use of cells placed on tissue scaffolds in the formation of new viable tissue for a medical purpose but is not limited to applications involving cells and tissue scaffolds. While it was once categorized as a sub-field of biomaterials, having grown in scope and importance it can be considered as a field in its own.

### Etymology

The historic origins of the term are unclear as the definition of the word has changed throughout the past decades. The term first appeared in a 1984 publication that described the organization of an endothelium-like membrane on the surface of a long-implanted, synthetic ophthalmic prosthesis.

The first modern use of the term as recognized today was in 1985 by the researcher, physiologist and bioengineer Y.C Fung of the Engineering Research Center. He proposed the joining of the terms tissue (in reference to the fundamental relationship between cells and organs) and engineering (in reference to the field of modification of said tissues). The term was officially adopted in 1987.

As time progresses and technology advances, there is a constant need for change in the approach researchers take in their studies. Tissue engineering has continued to evolve over centuries. In the beginning people used to look at and use samples directly from human or animal cadavers. Now, tissue engineers have the ability to remake many of the tissues in the body through the use of modern techniques such as microfabrication and three-dimensional bioprinting in conjunction with native tissue cells/stem cells. These advances have allowed researchers to generate new tissues in a much more efficient manner. For example, these techniques allow for more personalization which allow for better biocompatibility, decreased immune response, cellular integration, and longevity. There is no doubt that these techniques will continue to evolve. We have continued to see microfabrication and bioprinting evolve over the past decade. In 1960, Wichterle and Lim were the first to publish experiments on hydrogels for biomedical applications by using them in contact lens construction. Work on the

field developed slowly over the next two decades, but later found traction when hydrogels were repurposed for drug delivery. In 1984, Charles Hull developed bioprinting by converting a Hewlett-Packard inkjet printer into a device capable of depositing cells in 2-D. Three dimensional (3-D) printing is a type of additive manufacturing which has since found various applications in medical engineering, due to its high precision and efficiency.

### Autologous

The donor and the recipient of the cells are the same individual. Cells are harvested, cultured or stored, and then reintroduced to the host. As a result of the host's own cells being reintroduced, an antigenic response is not elicited. The body's immune system recognizes these re-implanted cells as its own, and does not target them for attack. Autologous cell dependence on host cell health and donor site morbidity may be deterrents to their use. Adipose-derived and bone marrow-derived mesenchymal stem cells are commonly autologous in nature, and can be used in a myriad of ways, from helping repair skeletal tissue to replenishing beta cells in diabetic patients.

Techniques for cell isolation depend on the cell source. Centrifugation and apheresis are techniques used for extracting cells from biofluids (e.g., blood). Whereas digestion processes, typically using enzymes to remove the Extracellular Matrix (ECM), are required prior to centrifugation or apheresis techniques to extract cells from tissues/organs. Trypsin and collagenase are the most common enzymes used for tissue digestion. While trypsin is temperature dependent, collagenase is less sensitive to changes in temperature.

With biologist James Thompson's development of first human stem cell lines in 1998 followed by transplantation of first laboratory-grown internal organs in 1999 and creation of the first bioprinter in 2003 by the University of Missouri when they printed spheroids without the need of scaffolds, 3-D bioprinting became more conventionally used in medical field than ever before. So far, scientists have been able to print mini organoids and organs-on-chips that have rendered practical insights into the functions of a human body. Pharmaceutical companies are using these models to test drugs before moving on to animal studies. However, a fully functional and structurally similar organ hasn't been printed yet. A team at University of Utah has reportedly printed ears and successfully transplanted those onto children born with defects that left their ears partially developed.

Today hydrogels are considered the preferred choice of bio-inks for 3-D bioprinting since they mimic cells' natural ECM while also containing strong mechanical properties capable of sustaining 3-D structures. Furthermore, hydrogels in conjunction with 3-D bioprinting allow researchers to produce different scaffolds which can be used to form new tissues or organs. 3-D printed tissues still face many challenges such as adding vasculature.

Meanwhile, 3-D printing parts of tissues definitely will improve our understanding of the human body, thus accelerating both basic and clinical research. The term has also been applied to efforts to perform specific biochemical functions using cells within an artificially-created support system (e.g. an artificial pancreas, or a bio artificial liver).

While most definitions of tissue engineering cover a broad range of applications, in practice the term is closely associated with applications that repair or replace portions of or whole tissues (i.e., bone, cartilage, blood vessels, bladder, skin, muscle etc.). Often, the tissues involved require certain mechanical and structural properties

for proper functioning. The term regenerative medicine is often used synonymously with tissue engineering, although those involved in regenerative medicine place more emphasis on the use of stem cells or progenitor cells to produce tissues.