

# Artificial tissues

## Artificial tissues

Artificial tissues are tissues created synthetically to replace damaged or non-functional patient tissue. However, this does not mean that this entire structure is artificial, it is only artificially created. As a building material, we use cells from the treated patient, from a donor of the same species or a donor of a different species. But we have to extract the cells, we can't make them. What we can make is the so-called scaffolding. This construction serves as a support for living cells that are implanted into it, they create an extracellular matrix, and thus their own environment, and they can now function without a scaffold, as a full-fledged tissue.

### Cells as structural material

Tissue engineering uses living cells as construction materials. For example, using live fibroblasts in skin replacement or repair or live chondrocytes in cartilage repair. Cells have been available as a building material since 1998, when scientists at the Geron Corporation discovered how to lengthen telomeres to produce non-ending cell lines. Before this discovery, laboratory cultures of healthy, non-cancerous mammalian cells divided only after a fixed number of repetitions until they reached the so-called Hayflick limit.

### Extraction

From liquid tissues such as blood, cells are usually obtained by centrifugation or apheresis. From solid tissues, extraction is more difficult. The tissue is first digested with trypsin or collagenase enzymes to remove the extracellular matrix in which the cells adhere. Free-floating cells can then be extracted again by centrifugation or apheresis. <sup>[1]</sup>

### Scaffold

The cells are usually implanted or "seeded" into an artificial structure capable of supporting three-dimensional tissue formation. These structures, usually called a scaffold, are often the deciding factor for successful implantation. They must be constructed in such a way that the implanted cells can influence their structure and thus create their own, natural microenvironment. The scaffold must meet certain requirements. High porosity and corresponding pore sizes are necessary to properly seat cells in the structure and allow diffusion of cells and nutrients. Biodegradability is also a very important factor, as the scaffold must be absorbed into the surrounding tissue without the need for surgical removal, so as not to disturb the newly formed tissue. The rate at which degradation occurs must match as closely as possible the rate of tissue formation. This means that when the cells make their own intercellular matrix, the scaffold is able to provide structural integrity in the tissue and eventually disintegrates, leaving the newly formed tissue to take over the mechanical load.

### Materials

Nanofibers of collagen and some polyesters are most often used in the construction of the carrier. Commonly used synthetic materials include PLA – polylactic acid. This polyester degrades in the human body to form lactic acid, which is naturally degradable. Similar materials are polyglycolic acid (PGA) and polycaprolactone (PCL). Collagen, chitosan, hyaluronic acid and fibroin are suitable natural materials. <sup>[2]</sup>

### Scaffold production (synthesis)

#### Textile Technology

These techniques include all steps that have been successfully used to produce "non-woven" networks of various polymers. In particular, polyglycolide nonwoven structures have been tested for tissue engineering. These fibrous structures have been found to be suitable for the growth of several different types of cells, but their disadvantage is excessive porosity and pore size regularity.

#### SCPL (Solvent Casting & Particulate Leaching)

This procedure enables the preparation of porous structures with regular porosity but limited thickness. First, the polymer is dissolved in a suitable organic solvent (e.g. polylactic acid is dissolved in dichloromethane), then the solution is cast into a mold filled with porogen particles. The porogen can be an inorganic salt such as sodium chloride or sucrose crystals, gelatin beads, or paraffin beads. The size of the porogen particles affects the pore size of the scaffold. After the polymer solution occupies the porogen particles, the solvent is allowed to completely evaporate, then the composite structure in the mold is immersed in a bath containing a liquid suitable for dissolving the porogen. In the case of sodium chloride, sucrose and gelatin it is water and in the case of paraffin an aliphatic solvent such as hexane. As soon as the porogen is completely dissolved, we get a separate porous structure. The disadvantage of the structures obtained by this method is that we can only obtain structures with a small thickness, and during production we must take care to completely remove the remains of the organic solvent that was used, because it could disturb the cells that we will implant in the scaffold.

## Gas Foam

This technique uses gas as a porogen. First, the disk structure of the desired polymer is prepared by pressing in a heated mold. These discs are then placed in a chamber where they are exposed to high CO<sub>2</sub> pressure for several days. The pressure inside the chamber gradually equalizes with the atmospheric pressure. During this process, the pores are created by carbon dioxide molecules, which gradually leave them, so that the scaffold has a sponge-like structure as a result. The main problems arising from this technique are the use of excessive heat during molding, which precludes the use of any thermally degradable material in the polymer matrix, and insufficient pore connectivity.

## Emulsification and freeze drying

This technique does not require the use of a solid porogen such as SCPL. First, the synthetic polymer is dissolved in a suitable solvent (e.g. polylactic acid in dichloromethane), then water is added to the solution and the two liquids form an emulsion. Before the two phases can separate, the emulsion is cast into a mold and quickly frozen by immersion in liquid nitrogen. The frozen emulsion is subsequently lyophilized to remove the dispersed water and solvent, leaving a solidified porous polymer structure in the mold. While emulsification and lyophilization allow faster preparation compared to SCPL because it does not require time-consuming leaching, it still requires the use of solvents. In addition, the pore size is relatively small and the porosity is often irregular. Lyophilization itself is also a commonly used technique for scaffold production. In particular, it is used to prepare spongy collagen structures. The collagen is dissolved in a solution of acetic acid or hydrochloric acid, the solution is then poured into a mold, frozen with liquid nitrogen and lyophilized.

## TIPS (Thermally Induced Phase Separation)

Similar to the previous technique, this phase separation procedure requires the use of a solvent with a low melting point, plus in this case the additional condition is that it must sublime easily. For example, dioxane, which is used to dissolve polylactic acid, is suitable. Subsequent phase separation is induced by adding a small amount of water, resulting in a polymer-poor phase and a polymer-rich phase. This is followed by cooling below the melting point of the solvent and vacuum drying, during which the solvent sublimates. With this procedure, we get a finished scaffold. This method has the same disadvantages as emulsification and lyophilization.

## Electrostatic

A highly versatile technique that can be used to produce continuous fibers from micrometers to nanometers. In a typical electrostatic setup, the solution is fed to a spinneret and a high voltage is applied to its tip. The build-up of electrostatic resistance within the charged solution causes a thin filament of current to form. Using a collector plate or rod with an opposite charge placed in the solution, continuous fibers are formed, from which a highly porous network is formed. The main advantages of this technique are its simplicity and variability. Under laboratory conditions, this method requires a voltage source of approximately 30 kV, a flat-tip syringe, and a conductive collector. By adjusting the conditions, for example, the distance of the collector, the magnitude of the applied voltage, or the flow rate of the solution, we can fundamentally change the construction of the scaffold.

## CAD / CAM technology

Most of the above techniques are limited in their ability to control porosity and pore size. With computer support, these design and manufacturing parameters can be checked. First, the three-dimensional structure is designed by CAD software. Porosity is regulated using software algorithms. The scaffold is then realized using inkjet printing, where polymer powder or polymer melt serves as "ink".

## Biosynthetic organs

If all therapeutic means fail and the function of the failing organ is no longer compatible with the patient's life, replacements of parts or whole organs are used. One option is the transplantation of tissues from other organisms, it is necessary to observe strict criteria (e.g. compatibility of blood group, previous history of the donor), subsequent, long-term, pharmacological support of immunosuppressants and modification of the regimen. Despite this, the success of transplant care is not guaranteed. Another possibility is the synthesis of parts or whole artificial organs.

Biosynthetic organs are artificially created devices that are implanted or integrated into the human organism for the purpose of replacing a non-functional original organ. Synthetic organs may not be directly related to the support of basic physiological functions, but they can greatly improve the recipient's quality of life. These organs are energetically independent, they do not require connection to an energy source (regular battery charging) or other stationary sources (filters, chemical supplements).

## Indication

Indications for the creation and implementation of such a body may be:

- support of basic vital functions and thus prevention of sudden death of the organism (e.g. artificial heart);
- rapid improvement of the patient's quality of life, restoration of self-sufficiency (e.g. artificial limb);
- improving the quality of social life (e.g. cochlear implants);
- cosmetic adjustments after cancer or injuries.

# Organs

## Heart

Implantation of the whole heart is performed in patients whose life is in immediate danger, despite the advanced possibilities of today's medicine, it was not possible to create a synthetic heart that would fully replace the function of the original organ for a period longer than 18 months. However, parts of the damaged myocardium are also replaced. For example, an artificial material is used to replace an insufficient valve, most often an alloy of noble metals and plastics. Such a valve is subject to mechanical wear and requires permanent anticoagulant treatment. Another part of the heart that is already replaced as standard is the primary heart pacemaker, i.e. the source of impulses that make the heart contract. The device can have the function of an implanted defibrillator or continuous stimulation.

## Brain

Despite the advanced possibilities of today's medicine, it was not possible to transplant the brain or its parts. However, various stimulators can be implanted in the brain, which by sending electrical impulses stimulate the brain tissue and thus eliminate the symptoms of various diseases, such as epilepsy, depression, tremors, or Parkinson's disease.

## Ear

Despite the fact that with artificial cochlear implants, the quality of sound perception is not restored to a physiological level, the patient is able to perceive the surrounding sounds and speech with them. Which has an undeniable meaning for the deaf. A cochlear implant is an electrical device that filters the sound of speech from the surrounding noise and converts the sound into electrical impulses, which are then sent to the middle ear on the auditory system.

## Trachea

The first synthetic trachea was produced in 2011 in Sweden. Stem cells were taken from the buttock of an oncology patient, supported with growth factors and implanted on a carrier in the shape of a physiological trachea.

## Liver

Research into artificial liver synthesis is still in early development. For now, only a provisional liver has been created, which will allow the damaged original organ to regenerate, or temporarily replace its function, before a transplant is possible. A synthetic liver is made from hepatocytes placed on a carrier.

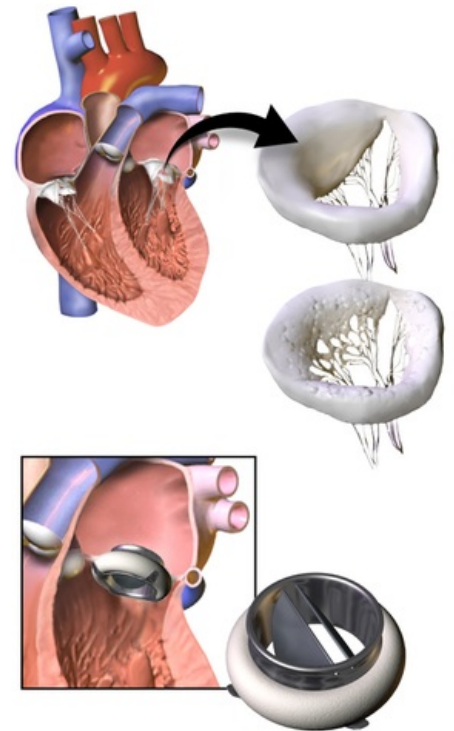
## Pancreas

The development of the synthetic pancreas is still in process. Some techniques use living cells of the islets of Langerhans embedded in carriers made of special materials, which would prevent the body's immune response and thus the destruction of the implanted functional cells. Pancreatic synthesis is particularly important for the treatment of diabetes.

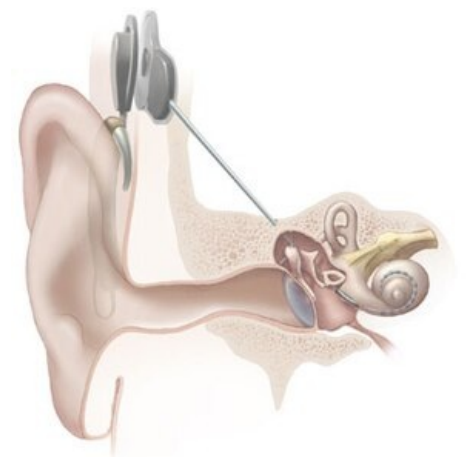
## Bladder

The main methods for replacing bladder function include either redirecting the flow of urine, creating a bladder in situ, or creating it from intestinal tissue.

## Corpus cavernosum



Heart valve



Cochlear implant

One of the treatment options for erectile dysfunction is the implantation of manually inflated balloons. Which is a very drastic and irreversible surgical method intended for those patients for whom all other types of treatment have already failed.

## Ovaries

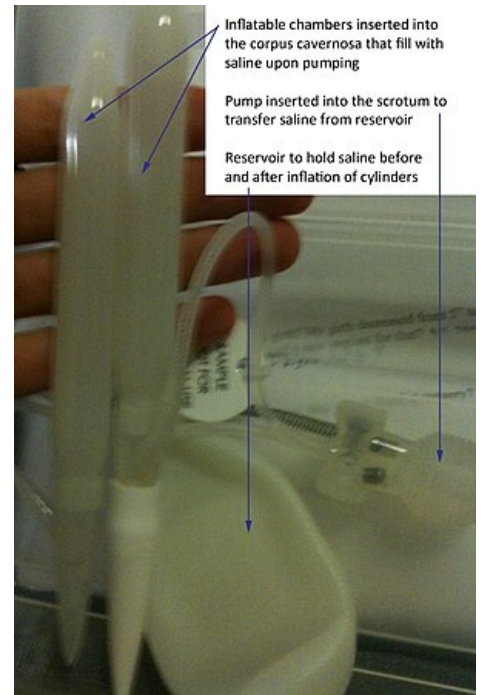
Women affected by cancer who have been exposed to chemotherapy or radiation often experience oocyte damage and early onset of menopause. Using 3D technology and a Petri dish, synthetic ovaries were created from the patient's own tissue, which are used for in vitro maturation of immature oocytes.

## Limbs

The effort to replace amputated limbs dates back to the Middle Ages. The original prostheses were heavy, uncomfortable, immobile and unsatisfactory. The development of limb replacements was pushed forward by the strife of the war. Nowadays, replacements are already of such high quality that an uninformed observer may not recognize the absence of the original limb at all. On the contrary, the advantages of using limb prostheses in sports compared to physiological limbs have been debated in recent years.

## Tissues

The synthetic production of tissues containing collagen is widespread. Laboratory-grown cartilage has already been successfully used in knee replacements. Synthetic skin, made from human skin cells embedded in hydrogel, is very beneficial in the treatment of burns. So far, artificial muscle tissue has been created in the form of edible animal flesh.



Drilling body implant

## Resources

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## References

1. [Tissue Engineering]
2. [Tissue Engineering]