Tissue Engineering and Regeneration in Dentistry

Definition of tissue engineering, and the status of it in Hungary, and in the international destinations

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SZÉCHENYI 2020

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Rules and timetable

Topic(s)
Course registration
-
Introduction, discussion of schedule **Definition of tissue engineering, and the status of it in Hungary, and in the international destinations** **Basics of tissue engineering and regeneration, implementation possibilities, and the classification of the applicable materials**
Inorganic scaffolds in tissue engineering (hydroxyapatite, tricalcium phosphate and calcium sulphate based systems…) **The application of polymer scaffolds in the tissue engineering and regeneration**
Nanotechnology in tissue engineering benefits and dangers in the field of dentistry **Biomimetic challenges and opportunities**

Rules and timetable II.

Topic(s)
Nanotechnology in tissue engineering benefits and dangers in the field of dentistry **Biomimetic challenges and opportunities**
The results of tissue engineering in dentistry and other medical field I. **The results of tissue engineering in dentistry and other medical field II.**
The role of cells in regeneration, cell-cell, and cell-scaffold interactions **Research on the topic of tissue engineering in UD Faculty of Dentistry, Dept. of Biomaterials and Prosthetic Dentistry**
Tissue engineering and regeneration in the field of oral surgery I-II.
Tissue engineering and regeneration in the field of periodontology. Written test

The Williams Definition of Biocompatibility

‘The ability of a material to perform with an appropriate host response in a specific application’

The Williams Dictionary of Biomaterials
Liverpool University Press, 1999

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Biomaterial

The Williams Definition (2009)

A biomaterial is a substance that has been engineered
to take a form which, alone
or as part of a complex system,
is used to direct, by control of interactions with
components of living systems,
the course of any therapeutic or diagnostic procedure.

The Williams Dictionary of Biomaterials
Liverpool University Press, 1999

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Definition of TE

Tissue engineering is the creation of new tissue for the therapeutic reconstruction of the human body, by the deliberate and controlled stimulation of selected target cells through a systematic combination of molecular and mechanical signals.

Williams D.F. On the mechanisms of biocompatibility, Biomaterials, 2008, 29, 2941
Williams D.F. On the nature of biomaterials, Biomaterials, 2009, 30, 5897

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Biocompatibility of Tissue Engineering

Scaffolds and Matrices

The biocompatibility of a scaffold or matrix for a tissue engineering product refers to the ability to perform as a substrate that will support the appropriate cellular activity, including the facilitation of molecular and mechanical signaling systems, in order to optimize tissue regeneration, without eliciting any undesirable local or systemic responses in the eventual host.

Previous FDA approval for the use of a biomaterial in a medical device is not an appropriate specification for a tissue engineering scaffold or matrix material

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Tissue engineering

Aims: Scaffold creation for remodelling of injured, or missing tissues; used by different cells, growth factors or any other materials what can promote this process.

Techniques: The combination of different organic, and inorganic, hydrophilic, and hydrophobic systems, used by various polymerization methodes.

Tools: Different tolerable polymers which could be degradable in appropiate conditions.

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Risks, and evaluations

We have to assess the biological risk before a device is used clinically

- ✓ We do not have high quality biomaterials for tissue engineering applications, and we need new test procedures
- ✓ The failure to produce clinical success with tissue engineering products is partly caused by the lack of standard testing and regulatory approval procedures
- ✓ Experience tells us the current pre-clinical test –mostly the cell based inverstigation procedures are definitely not predictive of clinical performance
- ✓ ISO 10993 is not a valid basis for testing new biomaterials

CONCLUSION:

We have to create effective procedures for quality control concerned with biological safety?

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Transplantation

In the USA in 2010 was 28600 transplantation
more than in the ¾ of the cases from dead donors
meanwhile more than 56000 new recipient was registered
nearly 7,000 patients died while wait for the transplantation

In Hungary in 2013 on the waiting list were
784 patient who wait for kidney, 124 for liver, 40 patient for heart and
9 patient had need for combined kidney- pancreas transplantation
Sum: 957
In contrast here were 355 organ-transplants from dead-donor, and
another 40 kidney-transplants were from living donor
Sum: 395

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Strategies

used by biodegradable matrix or inorganic scaffold

- Conduction of the repair process,
  isolation from the environment
- Induction of the repair process,
  bioactive materials
- Purposeful induction of repair process ,
  not only bioactive materials, but the cells
  (stem cells) were added
  (guided e.g. to soft tissues, or bone tissues)

Requirements to tissue (bone) scaffold materials

Biocompatibility:
The ability to work in an appropriate host , not triggered negative response .
Osseointegration:
Chemically connection can create between the material and tissue. (bioactivity)
Biodegradability:
The material can degradable/vanish, and new tissue can growth in this space .
Osseoconductivity:
The material can support the bone.
Osseoinduction:
The ability to induce differentiation of the cells to an osteoblastic phenotype .
Osseogenesis:
New bone creation in the present of greaft material.

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ANZ J Surg 2001;71:354; J Mater Chem 2010;20:8747;
J Mater Chem B 2013;1:1081.

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Possibilities to replacement of extensive local bone

	Advanteges	Disadvantages
Autograft	Standard	Limited availability the graft
Allograft	Same species, so similar structure, without osteoblasts	Postoperative infections, Risk of fracture, or any other infection/disease transmission
Xenograft	Easy availability, adequate source	Immunogenic properties/rejection/virus infection
Alloplastic graft	Availability, sterility	In the most of cases the lack of osteoinduction

ANZ J Surg 2001;71;354

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Alloplastic grafts

Ideal synthetic bone graft substitutes

Good mechanical properties “load-bearing”

Long term degradability to prevent fatigue fractures

Promoting bone formation (“osteogenesis”).

Bohner M. et al. J Eur Ceram Soc 2012;32:2663

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Examples for products

Examples for hydroxiapatite based commercial products:

PepGen ®

Cerabone ®

Ostim ®

BioOss ®

Tutoplast ®

Examples for β-Tricalcium phosphate ceramics containing commercial products:

Bioresorb ®

Chronos ®

Ceros ®

Cerasorb ®

Vitoss ®

Tadic D, Epple M. Biomaterials 2004;25:987

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Solid graft materials

- Inorganic materials
  - Calcium-phosphate (β–TCP), hydroxyapatite, silicates, sulfates
- Organic components
  - Natural materials
    (collagene, fibrin fibers, etc.)
  - Polymers (synthetic or natural)
    (natural: glycolic-acid, lactic-acid, hyaluronic acid, etc.
    synthetic: poly-urethane, poly-methyl-methacrylic acid)
- Composites

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Polymers, as scaffolds

Different polymers and co-polymers for solid scaffold:

Poly-(DL-lactic acid) PLA

Poly-(L-lactic acid) PLLA

Poly-(Lactic-co-glicolic acid) PLGA

Poly-(propylene glicol fumarate) PPF

Poly- (DL-lactic acid)-co-poly-(ethylene glycol)-mono-methoxy ether

PEG-PLA

Biotin functionalized PEG-PLA

Material variables

- Bulk material composition, microstructure, morphology,
- Crystallinity and crystallography,
- Elastic constants, compliance,
- Surface chemical composition, chemical gradient, molecular mobility,
- Surface topography and porosity
- Water content, hydrophobic – hydrophilic balance, surface energy
- Corrosion parameters, ion release profile, metal ion toxicity
- Polymer degradation profile, degradation product toxicity
- Leachables, catalysts, additives, contaminants
- Ceramic dissolution profile
- Wear debris release profile, particle size
- Sterility and endotoxins

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Host response characteristics

- Protein adsorption and desorption characteristics
- Complement activation
- Platelet adhesion, activation and aggregation
- Activation of intrinsic clotting cascade
- Neutrophil activation
- Fibroblast behaviour and fibrosis
- Macrophage activation, foreign body giant cell production
- Microvascular changes
- Osteoblast / osteoclast responses
- Endothelial proliferation
- Antibody production, lymphocyte behaviour
- Acute hypersensitivity / anaphylaxis
- Delayed hypersensitivity
- Genotoxicity, reproductive toxicity
- Tumour formation

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THANK YOU FOR YOUR ATTENTION!

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