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From bench to application: Current practices in tissue engineering and its realisation at maxillofacial units in Germany, Austria and Switzerland

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ABSTRACT

Over the last 20 years, the highly interdisciplinary field of tissue engineering (TE) has become an established subspecialty in research facilities all over the world. Numerous methods and protocols are available for various research intentions and aims, but there are no data indicating which of these methods and resources are generally used. This study is an overview of the resources and methods that are commonly applied in TE research in general, and in the field of oral and maxillofacial surgery (OMFS) in Germany, Austria and Switzerland.

The DÖSAK collaborative group for TE developed a detailed questionnaire and collected information from participating university hospitals in these three countries. We evaluated the availability of research facilities, *in vitro* realisation and *in vivo* designs for animal studies in these departments.

11 units who replied, out of 35 we contacted, conducted research on bone regeneration in interdisciplinary research facilities. 10 departments used xenogeneic and alloplastic scaffolds for *in vitro* and *in vivo* applications. In this case, the most commonly utilised trademarks were Bio-Oss® and CERASORB®.

9 units used osteoblasts (73%) and 10 proliferation assays *in vitro*, whereas rats served as the standard animal model for histology/immunohistochemistry in 6. All research units were interested in establishing a platform for research exchange and communication.

This study shows that tissue engineering is well established and highly accepted in most participating university hospitals and research facilities. The presented data, together with data published in a foregoing paper will help arrange more readily available standardised procedures for further investigations.

1. Introduction

Tissue engineering (TE) techniques can be used to produce regenerative soft and hard tissues for almost all clinical applications. The aim of TE technologies is to replace or compensate for lost or damaged tissue and potentially provide fully functional organ replacements.

The field of TE can be seen as one of the most important interdisciplinary research areas in 21st century clinical medicine, with enormous potential for growth (Bertram et al., 2012; Fischer et al., 2011; Lysaght and Reyes, 2001; Lysaght and Hazlehurst, 2004; Lysaght et al., 2008).

Generally, TE research requires four conceptional abutments: cells, scaffolds, cell medium and proteins (e.g. growth factors) (Fig. 1). However, given the provision of these materials, TE research still requires large investments of time and finances.

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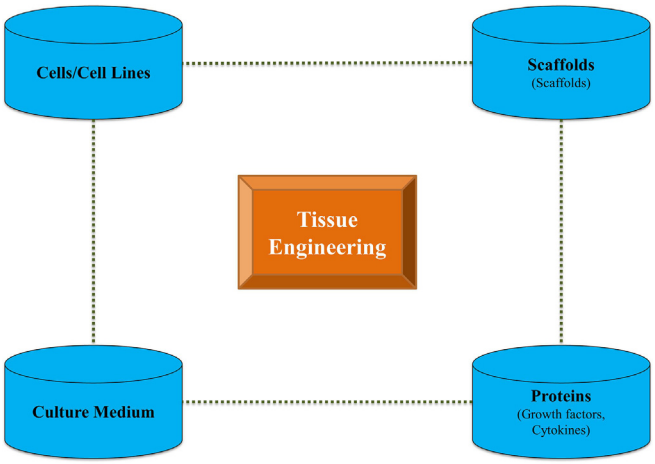

Fig. 1. The four pillars of TE.

Although numerous research articles and reviews describe specialised and general concepts in this field, information regarding fundamental research methods and research intentions of hospitals, laboratory groups and scientists is unavailable. Such information is a prerequisite for efficient interdisciplinary research platforms (Bertram et al., 2012; Chen et al., 2012; Fischer et al., 2011; Kolk et al., 2012; Payne et al., 2013; Sivayoham et al., 2013; Sterodimas et al., 2010; Susarla et al., 2011; Wood and Mealey, 2012).

The purpose of this study was to evaluate current practices and general TE research methods in the field of oral and maxillofacial surgery (OMFS) in Germany, Austria and Switzerland.

2. Materials and methods

We distributed our questionnaires to 35 university hospitals selected from the German, Austrian and Swiss Association of Oral and Maxillofacial Surgeons database of oral and maxillofacial hospital units.

The standardised multiple-choice questionnaire was developed by the DÖSAK collaborative group for TE to characterise TE research. Multiple choices were allowed as indicated above the table bars, and 17 questions were used to assess general information, *in vitro* realisation and *in vivo* realisation as follows:

- General information: main research interests, experimental systems used, number and types of laboratories used, relative importance to daily research, scaffolds/carriers used, preferred alloplastic materials and their manufacturers, and customary alloplastic scaffolds used.
- *In vitro* realisation: preferred cells/cell lines, types and purposes of tests for cell behaviours. As usual in a scientific context, the term “cell lines” was used for osteoblasts, endothelial cells, odontoblasts, gingival fibroblasts, keratinocytes, adipocytes and osteoclasts. In contrast “cells” only stands for mesenchymal stem cells (MSC).
- *In vivo* realisation: established animal models, transgenic animals, analytical methods and technologies and *in vivo* histology, use of Technovit preparations for immunohistochemical examinations, interest in a platform for interchange and communication.

The survey questionnaire was mailed to executive staff members of each department during the 16 months between January 2010 and April 2011.

2.1. Data analysis

The central goal was a free cross-sectional baseline study of the research situation in the field of TE within the affiliated countries to obtain only descriptive data. As standard in any form of study with detection character quantitative data were coded in accordance to SPSS, numerically evaluated and then transferred to further graphical processing. Graphical presentation were generated using Graphpad Prism 6 (GraphPad Software Inc., 2236 Avenida de la Playa, La Jolla, CA 92037, USA).

3. Results

A total of 11 university hospitals completed the questionnaire (response rate, 31.4%). The numbers of answers per item constituted the ratio of all participating hospitals ($n = 11$).

3.1. General information

The main research interest was bone regeneration (10), followed by skin transplantation (3), mucosal transplantation (2), teeth regeneration (2) and nerve regeneration (1). No interest in muscle or other tissue regeneration was registered (Table 1). The numbers of research areas studied in single departments varied from 0 ($n = 1$) to 5 ($n = 1$), with most hospitals concentrating on one research area ($n = 7$; Table 1).

Eight hospitals used *in vitro* and *in vivo* systems for their experiments, two used only *in vitro* systems, and one university used neither systems, corresponding with 10 using *in vitro* systems, and 9 using *in vivo* systems.

Most units used interdisciplinary research facilities (8) and/or their own laboratories (6), whereas four used external amenities. Two hospitals used all kinds of research facilities (2), three used only two types of research facilities and five primarily used interdisciplinary laboratories.

When asked to rate percentage importance of tissue engineering in daily research routines, 3 hospitals answered 50–70%, another 3 indicated 10–20% and the other three hospitals answered 70–90%, 30–50% and 0–10%, respectively (Fig. 2).

The majority of university hospitals (8) used alloplastic and xenogenic scaffolds for tissue engineering research, whereas 6 used autologous materials and 1 used allogeneic supplies (Table 2). When working with alloplastic materials, 6 used ceramics and 2 worked with plastics, textiles and other materials. Out of these, 5 were self-manufactured and 9 were purchased.

Among marketed materials, 6 units preferred Bio-Oss® (Geistlich, Wolhusen, Switzerland) and CERASORB® (curasan AG, Kleinostheim, Germany) scaffolds, and 5 used other carrier systems.

3.2. In vitro realisation

Preferences for cell lines were 9 for osteoblasts, 5 for endothelial cells and odontoblasts and 4 for mesenchymal stem cells. Other cell lines included gingival fibroblasts (2), keratinocytes (2), adipocytes

Table 1
Main research interests.

	Number of answers	Percentage ratio in all hospitals	Number of research areas	Number of hospitals
Bone regeneration	9	82	5	1
Nerve regeneration	1	9	3	1
Skin transplants	3	27	2	1
Mucosal transplants	2	18	1	7
Muscle regeneration	0	0	0	1
Teeth regeneration	2	18		
Others	0	0		

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