maxgraft® & CHB Spongiosa available scientific and clinical documents

Facts

- Processed human tissue, two exclusive tissue bank cooperations
- so far no serious clinical complication or objection
- approx. 34,000 successful dental clinical treatments & 300,000 ortho-trauma-spine surgeries (03/2015)
- no product related recall or remark
Summary and Conclusion of scientific and clinical projects (selection):

Reviews/Overviews

- Tissue and cell therapy is a field in which intense worldwide exchange is taking place. The European Community has therefore guaranteed to achieve the highest possible level of protection to safeguard public health regarding quality and safety of tissues and cells. The relevant Directive 2004/23/EC of the European Parliament and of The Council on Setting Standards of ‘Quality and Safety for the Donation, Procurement, Testing, Processing, Preservation, Storage and Distribution of Human Tissues and Cells’ and their complementary Directives 2006/17/EC and 2006/86/EC are now implemented into national law in the countries of the European Union.

Physico-Chemical-Biological Research

- High-dose electron beam sterilization of soft-tissue grafts maintains significantly improved biomechanical properties compared to standard gamma treatment.
- Thermodisinfection of human femoral heads from living donors harvested during hip joint replacement is an established processing procedure. This study was designed to examine the influence of heat sterilization on pull out strength of cancellous bone and storage at different temperatures up to 2 years since we had previously studied the storage of unprocessed cancellous bone.
- Bone transplantation is frequently used for the treatment of large osseous defects. The availability of autologous bone grafts as the current biological gold standard is limited and there is a risk of donor site morbidity. Allogenic bone grafts are an appealing alternative, but disinfection should be considered to reduce transmission of infection disorders.

Clinical Research

- Comparison of mineralized cancellous bone allograft (Puros) and anorganic bovine bone matrix (Bio-Oss) for sinus augmentation: histomorphometry at 26 to 32 weeks after grafting.

Case Reports

- Single-surgery implant placement using maxillary sinus augmentation and allograft bone rings.
- Ridge augmentation using customized allogenic bone blocks: proof of concept and histological findings.
- Simplified onlay grafting with a 3-dimensional block technique: A technical Note.

Other clinical fields of use & comparable product

- Effect of guided bone regeneration with or without pericardium bioabsorbable membrane on bone formation.
- In vivo and in vitro comparison of three different allografts vitalized with human mesenchymal stromal cells.
- Comparison of six bone-graft substitutes regarding to cell seeding efficiency, metabolism and growth behaviour of human mesenchymal stem cells (MSC) in vitro.
Current trends in tissue banking.

Pruss A\textsuperscript{1}, Kalus U.

Tissue and cell therapy is a field in which intense worldwide exchange is taking place. The European Community has therefore guaranteed to achieve the highest possible level of protection to safeguard public health regarding quality and safety of tissues and cells. The relevant Directive 2004/23/EC of the European Parliament and of The Council on Setting Standards of ‘Quality and Safety for the Donation, Procurement, Testing, Processing, Preservation, Storage and Distribution of Human Tissues and Cells’ and their complementary Directives 2006/17/EC and 2006/86/EC are now implemented into national law in the countries of the European Union. Alongside harmonized documentation of anamnesis and medical histories, testing for infection markers has always been of particular interest to physicians and regulators. Production and examination of tissue preparations have been adapted to the guidelines issued by authorities and specialist associations in the respective fields (musculoskeletal tissues, corneal tissue, heart valves), and evidence-based indication for transplantation has been discussed. In the present issue of Transfusion Medicine and Hemotherapy the reader is introduced to current facets of tissue banking seen from scientific points of view.


Clinical efficacy and compatibility of allogeneic avital tissue transplants sterilized with a peracetic acid/ethanol mixture

Axel Pruss, Carsten Perka, Petra Degenhardt, Ute Maronna, Karin Büttner-Janz, Bodo Paul, Klaus Müller, Christoph Klumpp, Johannes C. Bruck & Rüdiger von Versen

Abstract

In the course of the past 20 years a quantity of approximately 60,000 allogeneic avital tissue grafts sterilized with the peracetic acid–ethanol method (PES) were transplanted successfully. Based on a retrospective report of clinical experience of the years 1997–2001 on the overall scope of tissue grafts manufactured by the Tissue Banks of the University Hospital Charité and the German Institute for Cell and Tissue Replacement, the clinical efficacy and side effects of 18.3\% (3.087/16.823) of all transplants were studied. Cancellous (1.601/3.087) and cortical (291/3.087) bone transplants as well as amnion (1.027/3.087) constituted the greatest part. In 91\% of the examined patients (2.369/2.592) tissue integration ratios ranging from good up to very well could be observed. The transplant function of defect replacement or of a spacer respectively could be obtained for all types of tissue. The clinical effect caused by the transplant resulted in more than 99\% of the transplants in primary integration or in the desired aim of the therapy (defect replacement, stabilization in case of palliative operations, etc.). In less than 1\% (9/2.592) of cases a secondary healing occurred for cancellous bone transplantations or, revisional operations became necessary. In all cases severe side effects, in particular transmission of infectious diseases or transplant rejections, were not observed.
Peracetic Acid-Ethanol Treatment of Allogeneic Avital Bone Tissue Transplants — a Reliable Sterilization Method
Axel Pruss, Ulf B Göbel, Georg Pauli, Moujahed Kao, Michael Seibold, Hans-Joachim Mönig, Arne Hansen, Rüdiger von Versen

Abstract:
Objectives. Based on the European Standard EN 1040, the validation guidelines of the German Federal Institute for Drugs and Medical Devices and CPMP guidelines we tested the antimicrobial effectiveness of a peracetic acid-ethanol sterilization procedure (PES) in allogeneic avital bone transplants. Study design. Delipidated human bone spongiosa cubes (15×15×15 mm) served as tissue. Three enveloped viruses (human immunodeficiency virus type 2, pseudorabies virus, bovine virus diarrhoea virus) and three non-enveloped viruses (hepatitis A virus, poliovirus, porcine parvovirus) were used. The reduction of virus infectivity was measured as TCID50/ml in neutralized supernatants and bone homogenates. Staphylococcus aureus, Enterococcus faecium, Pseudomonas aeruginosa, Bacillus subtilis, Clostridium sporogenes, Mycobacterium terrae, Candida albicans, Aspergillus niger as well as spores of Bacillus subtilis were tested additionally. PES led to a reduction of virus titres by more than 4 log10. Only HAV showed a reduction below 4 log10 (2.87) with residual infectivity. After including a delipidating step for HAV-infected cells, a reduction of over 7 log10 HAV titre was found. For viable bacterias, fungi and spores a titre reduction below the detection level (5 log10) was achieved after an incubation time of 2 hours. Conclusions. The peracetic acid-ethanol procedure proved to be a reliable method for the sterilization of human bone transplants (layer thickness ≥ 15 mm). However, additional safety measures (anamnestic informations, infectious serology, HIV-/HBV-/HCVPCR in case of multiorgan donors) should be taken.

Physico-Chemical-Biological Research


High-dose electron beam sterilization of soft-tissue grafts maintains significantly improved biomechanical properties compared to standard gamma treatment.
Hoburg A1, Keshlaf S, Schmidt T, Smith M, Gohs U, Perka C, Pruss A, Scheffler S.

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Abstract

Allografts have gained increasing popularity in anterior cruciate ligament (ACL) reconstruction. However, one of the major concerns regarding allografts is the possibility of disease transmission. Electron beam (Ebeam) and Gamma radiation have been proven to be successful in sterilization of medical products. In soft tissue sterilization high dosages of gamma irradiation have been shown to be detrimental to biomechanical properties of grafts. Therefore, it was the objective of this study to compare the biomechanical properties of human bone-patellar tendon-bone (BPTB) grafts after ebeam with standard gamma irradiation at medium (25 kGy) and high doses (34 kGy). We hypothesized that the biomechanical properties of Ebeam irradiated grafts would be superior to gamma irradiated grafts. Paired 10 mm-wide human BPTB grafts were harvested from 20 donors split into four groups following irradiation with either gamma or Ebeam (each n = 10): (A) Ebeam 25 kGy,
Gamma 25 kGy, Ebeam 34 kGy (D) Gamma 34 kGy and ten non-irradiated BPTB grafts were used as controls. All grafts underwent biomechanical testing which included preconditioning (ten cycles, 0-20 N); cyclic loading (200 cycles, 20-200 N) and a load-to-failure (LTF) test. Stiffness of non-irradiated controls (199.6 ± 59.1 N/mm) and Ebeam sterilized grafts did not significantly differ (152.0 ± 37.0 N/mm; 192.8 ± 58.0 N/mm), while Gamma-irradiated grafts had significantly lower stiffness than controls at both irradiation dosages (25 kGy: 126.1 ± 45.4 N/mm; 34 kGy: 170.6 ± 58.2 N/mm) (p < 0.05). Failure loads at 25 kGy were significantly lower in the gamma group (1,009 ± 400 N), while the failure load was significantly lower in both study groups at high dose irradiation with 34 kGy (Ebeam: 1,139 ± 445 N, Gamma: 1,073 ± 617 N) compared to controls (1,741 ± 304 N) (p < 0.05). Creep was significantly larger in the gamma irradiated groups (25 kGy: 0.96 ± 1.34 mm; 34 kGy: 1.06 ± 0.58 mm) than in the Ebeam (25 kGy: 0.50 ± 0.34 mm; 34 kGy: 0.26 ± 0.24 mm) and control (0.20 ± 0.18 mm) group that did not differ significantly. Strain difference was not different between either control or study groups (controls: 1.0 ± 0.03; Ebeam 34 kGy 1.04 ± 0.018; Gamma 34 kGy 1.0 ± 0.028; 25 kGy: 1.4 ± 2.0; 34 kGy: 1.1 ± 1.1). The most important result of this study was that ebeam irradiation showed significantly less impairment of the biomechanical properties than gamma irradiation. Considering the results of this study and the improved control of irradiation application with electronic beam, this technique might be a promising alternative in soft-tissue sterilization.

Cell Tissue Bank. 2014 Apr 2. [Epub ahead of print]

Influence of thermodisinfection and duration of cryopreservation at different temperatures on pull out strength of cancellous bone.

Author information

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Abstract

Thermodisinfection of human femoral heads from living donors harvested during hip joint replacement is an established processing procedure. This study was designed to examine the influence of heat sterilization on pull out strength of cancellous bone and storage at different temperatures up to 2 years since we had previously studied the storage of unprocessed cancellous bone. Porcine cancellous bone resembling human bone structure was obtained from 140 proximal humerus of 6-8 months old piglets. Pull out strength of screws after thermodisinfection was compared with unprocessed cancellous bone and tested immediately and after 6, 12 and 24 months of storage at -20 and -80 °C. A three-way ANOVA was performed and significance level was 5 %. The thermodisinfect ed bone showed a pull out force of 2729 N (1657-3568 N). The reduction of pull out strength compared with unprocessed bone over all periods of storage was 276 N on average with 95 % confidence interval ranging from 166 N to 389 N (p < 0.0001). Different freezing temperatures did not influence this mechanic property within 24 months storage and showed no difference compared with fresh frozen bone. Thermodisinfection of cancellous bone preserves tensile strength necessary for clinical purposes. The storage at -20 °C for at least 2 years did not show relevant decrease of pull out strength compared with -80 °C without difference between thermodisinfect ed and fresh frozen bone. The increase of the storage temperature to -20 °C for at least 2 years should be considered.

Comparative biomechanical and microstructural analysis of native versus peracetic acid-ethanol treated cancellous bone graft.

Rauh J¹, Despang F², Baas J³, Liebers C⁴, Pruss A⁴, Gelinsky M³, Günther KP¹, Stiehler M¹.

Abstract

Bone transplantation is frequently used for the treatment of large osseous defects. The availability of autologous bone grafts as the current biological gold standard is limited and there is a risk of donor site morbidity. Allogeneic bone grafts are an appealing alternative, but disinfection should be considered to reduce transmission of infection disorders. Peracetic acid-ethanol (PE) treatment has been proven reliable and effective for disinfection of human bone allografts. The purpose of this study was to evaluate the effects of PE treatment on the biomechanical properties and microstructure of cancellous bone grafts (CBG). Forty-eight human CBG cylinders were either treated by PE or frozen at -20 °C and subjected to compression testing and histological and scanning electron microscopy (SEM) analysis. The levels of compressive strength, stiffness (Young's modulus), and fracture energy were significantly decreased upon PE treatment by 54%, 59%, and 36%, respectively. Furthermore, PE-treated CBG demonstrated a 42% increase in ultimate strain. SEM revealed a modified microstructure of CBG with an exposed collagen fiber network after PE treatment. We conclude that the observed reduced compressive strength and reduced stiffness may be beneficial during tissue remodeling thereby explaining the excellent clinical performance of PE-treated CBG.

Author information

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Clinical Research


Case Reports


Dr. Sebastian Stavar, Dr. Rasmus Sperber (2013). Individuell-gefräster Knochenblock als Alternative zu Knochenersatzmaterialien. Dental Barometer 06/2013. (Clinical case maxgraft bonebuilder)

Dr. Markus Schlee, Dr. Yasmin Buchäckert (2013). Augmentation mit einem individuell gefrästen Knochentransplantat. DIGITAL_DENTAL.NEWS 03/2013. (Clinical case maxgraft bonebuilder)

Dr. Stephan Beuer (2012). Eine schonende Methode im atrophierten Kieferkamm (Augmentation mit allogenem, gefrästen Knochen). J CONT DENT EDUC 05/2012. (Clinical case maxgraft bonebuilder)

Helmut Hildebrandt, Mathias Fajen (†), Markus Schlee, Peter Neumeier, Sebastian Sauerbier (2012). Augmentation ausgedehnter horizontaler und vertikaler Defekte des Kieferkamm (Methoden und Fallbeispiele). Praktische Implantologie und Implantatprothetik (pip) 03/2012. (Clinical case maxgraft bonebuilder)


Dr. Andrea Grandoch, Dr. Ludwig Bogner, Dr. Dr. Peter Ehrl (2013). Resultatorientierte 3D-Implantations- und Augmentationsplanung. BDIZ EDI konkret 02/2013. (Clinical case maxgraft bonebuilder)


Papagiannoulis N, Agerakis E Steigmann M. Neues Implantatsystem, moderne Biomaterialien und innovative Techniken zur prothetischen Rehabilitation eines anspruchsvollen Falles. DENT IMPLANTOL 17, 1, 22 - 35 (2013) Clinical case; maxgraft, Cerabone, maxresorb, Jason membrane
Other Clinical Fields of Use or Comparable Products


Effect of guided bone regeneration with or without pericardium bioabsorbable membrane on bone formation.
Ahn YS¹, Kim SG, Kim CS, Oh JS, Lim SC.

Author information

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Abstract

**OBJECTIVE:**

The purpose of this study was to evaluate bone formation after using allogeneic bone alone or with a membrane.

**STUDY DESIGN:**

Bone graft was performed using the allograft Tutoplast, mineralized cancellous bone allograft, and pericardium in calvarial defects of 60 rats. Rats were divided in 3 groups: control group (no bone graft), group 1 (bone graft without membrane), and group 2 (bone graft with membrane).

**RESULTS:**

The most new bone formation occurred in group 2. After 6 weeks, group 2 showed infiltration of inflammatory cells, and inflammatory cells were still observed after 12 weeks. The membrane remained even after 12 weeks, and the membrane facilitated bone regeneration by blocking connective tissue.


In vivo and in vitro comparison of three different allografts vitalized with human mesenchymal stromal cells.


Author information

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Abstract

Bone allografts are commonly used by orthopedists to provide a mechanical support and template for cellular colonization and tissue repair. There is an increasing demand for bone graft substitutes.
that are safe and easy to store but which are equally effective in supporting new bone growth. In this study, we compared three different human bone allografts: (1) the cryopreserved allograft (frozen), (2) the gamma-irradiated and cryopreserved allograft (γ-irradiated), and (3) the solvent dehydrated and γ-irradiated-processed bone allograft (Tutoplast® Process Bone [TPB]). Human mesenchymal stromal cells (hMSCs) have the potential to differentiate into osteogenic, chondrogenic, and adipogenic lineages. Our results showed that hMSC seeding efficiency was equivalent among the three bone allografts. However, differences were observed in terms of cell metabolism (viability), osteoblastic gene expression, and in vivo bone formation. Frozen allografts had the higher frequency of new bone formation in vivo (89%). Compared with frozen allografts, we demonstrated that TPB allografts allowed optimal hMSC viability, osteoblastic differentiation, and bone formation to occur in vivo (72%). Further, the frequency of successful bone formation was higher than that obtained with the γ-irradiated allograft (55%). Moreover, after hMSC osteoinduction, 100% of the TPB and frozen allografts formed bone in vivo whereas only 61% of the γ-irradiated allografts did. As healthcare teams around the world require bone-grafting scaffolds that are safe and easy to store, the TPB allograft appears to be a good compromise between efficient bone formation in vivo and convenient storage at room temperature.


Comparison of six bone-graft substitutes regarding to cell seeding efficiency, metabolism and growth behaviour of human mesenchymal stem cells (MSC) in vitro.

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Abstract

INTRODUCTION:

Various synthetic bone-graft substitutes are used commercially as osteoconductive scaffolds in the treatment of bone defects and fractures. The role of bone-graft substitutes is changing from osteoconductive conduits for growth to a delivery system for biologic fracture treatments. Achieving optimal bone regeneration requires biologics (e.g. MSC) and using the correct scaffold incorporated into a local environment for bone regeneration. The need for an unlimited supply with high quality bone-graft substitutes continue to find alternatives for bone replacement surgery.

MATERIALS AND METHODS:

This in vitro study investigates cell seeding efficiency, metabolism, gene expression and growth behaviour of MSC sown on six commercially clinical available bone-graft substitutes in order to define their biological properties: synthetic silicate-substituted porous hydroxyapatite (Actifuse ABX), synthetic alpha-TCP (Biobase), synthetic beta-TCP (Vitoss), synthetic beta-TCP (Chronos), processed human cancellous allograft (Tutoplast®) and processed bovines hydroxyapatite ceramic (Cerabone). 250,000 MSC derived from human bone marrow (n=4) were seeded onto the scaffolds, respectively. On days 2, 6 and 10 the adherence of MSC (fluorescence microscopy) and cellular activity (MTT assay) were analysed. Osteogenic gene expression (cbfa-1) was analysed by RT-PCR and scanning electron microscopy was performed.

RESULTS:
The highest number of adhering cells was found on Tutoplast (e.g. day 6: 110.0+/−24.0 cells/microscopic field; p<0.05) followed by Chronos (47.5+/−19.5, p<0.05), Actifuse ABX (19.1+/−4.4), Biobase (15.7+/−9.9), Vitoss (8.8+/−8.7) and Cerabone (8.1+/−2.2). MSC seeded onto Tutoplast showed highest metabolic activity and gene expression of cbfa-1. These data are confirmed by scanning electron microscopy. The cell shapes varied from round-shaped cells to wide spread cells and cell clusters, depending on the bone-graft substitutes. Processed human cancellous allograft is a well-structured and biocompatible scaffold for ingrowing MSC in vitro. Of all other synthetical scaffolds, beta-tricalcium phosphate (Chronos) have shown the best growth behaviour for MSC.

DISCUSSION:

Our results indicate that various bone-graft substitutes influence cell seeding efficiency, metabolic activity and growth behaviour of MSC in different manners. We detected a high variety of cellular integration of MSC in vitro, which may be important for bony integration in the clinical setting.