DELIVERABLE REPORT

Grant Agreement Number: 242175 (FP7-HEALTH-2009-single-stage)
Collaborative project

VascuBone
Construction kit for tailor-made vascularized boneimplants

Deliverable 9.3: Conference Booklet

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Project coordinator organisation name Fraunhofer Gesellschaft
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CONFIDENTIAL

Version 1.0

Dissemination Level of Report

PU	Public	x
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

Abstract

This report on Deliverable 9.3 “Conference Booklet” is presented. This conference booklet is the second flyer in VascuBone summarizing the results achieved during VascuBone project time. It is part of the dissemination and exploitation plan described in Deliverable 9.5. and is part of the topic: advertisement, visibility, public relation of VascuBone for broader public.

The Conference Booklet serves as tool to demonstrate the activities and outcome of the research and work realised by the partners in VascuBone. On 6 pages the aim, expertise and contribution of each organisation is described. Additionally a blank template is available as insert. Each partner can show his current or updated news supplementary.

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1 Conference Booklet

In Deliverable Report 9.4 and 9.5 structures for the controlled dissemination of scientific results have been described. In Deliverable Report 9.5 all publications in peer-reviewed journals and participations at scientific conferences/workshops, fairs and symposia are listed in tables. To address the scientific community, policy makers and the interested public a conference booklet was designed promoting the VascuBone work, outcomes and partners to a broader public.

1.1 Content of the flyer

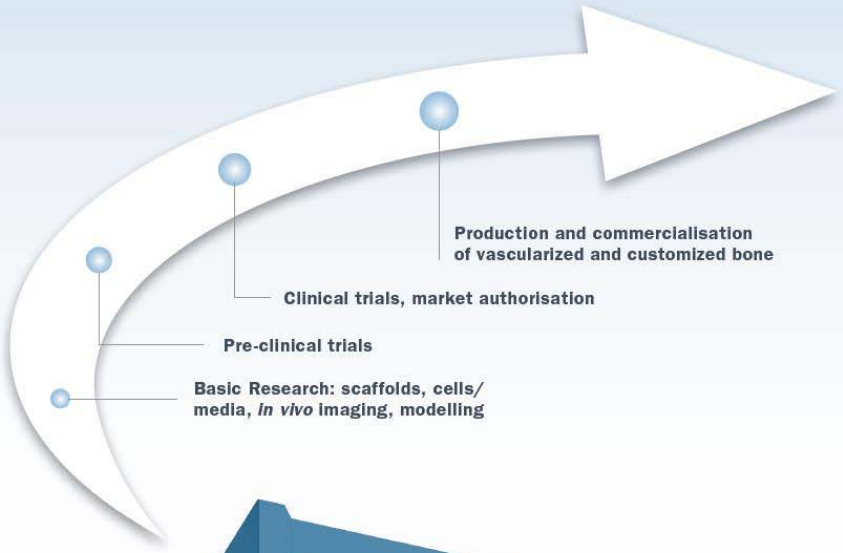
In the half time of VascuBone a post card-like flyer has been created and provided to the partners for distribution on conferences, fairs and workshops. At the end of VascuBone a more comprehensive Conference Booklet was designed, developed and finalized for further promotion especially with respect to build up a network of European clinics as end users of the developed VascuBone implants.

The first page is the eye-catcher with clear focus on the aim of VascuBone – the toolbox for bone regeneration. The next page describes the VascuBone project in general, followed by four pages presenting the partners, their expertise and contribution in the project.

1.1.1 Design and print version of the Conference Booklet

It was decided to implement the letterfold/trifold:

In the following figures the Conference Booklet is shown in single page format, starting with page one to six.



www.vascubone.eu

VascuBone

VascuBone – The Goal

The goal of VascuBone (2010 to 2014) was the development of a "toolbox" for bone regeneration, which on the one hand fulfills basic requirements and on the other hand is freely combinable with what is needed in the respective patient's situation. The toolbox includes a variety of biocompatible biomaterials and cell types, material modification technologies as well as simulations and analytical tools like molecular imaging-based *in vivo* diagnostics, which can be combined for the specific medical need. This toolbox can be used to develop translational approaches for regenerative therapies of different types of bone defects. The chosen bone diseases differ in their requirements, to ensure a successful implementation and translation. Additionally, this implementation strategy is characterized by high complexity to remove bottlenecks and limitations of bone regeneration identified in the clinical setting.

SEVENTH FRAMEWORK PROGRAMME

The research leading to these results has received funding from European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement n° 242175.

VascuBone – The Partners

Toolbox: biomaterials

The efficiency of bone regeneration is severely challenged in the case of large defects (>1cm) or healing disorders associated with e.g. age-related healing impairment, diabetes or radiation therapy. All of these conditions lead to an insufficient vascular repair process causing hypoxia and, thus, decreased bone formation in the injured area.

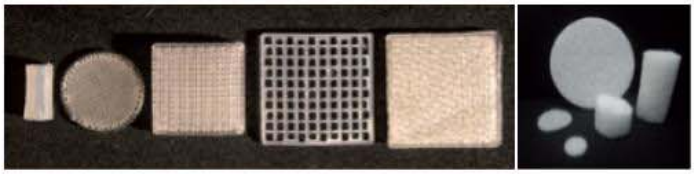
Royal Institute of Technology (KTH), Sweden

Scaffold-based therapies aiming at successful engineering of bone constructs for clinical use. AUXICELL™, degradable porous 3D scaffolds, are designed to elicit specific cellular responses at the molecular level.

Our strategy is to tune material-cell interactions:

- Functionalize polymers and immobilize growth factors
- Modify the surface and the mechanical properties with nano-diamond particles
- Optimize the scaffold production procedure

AUXICELL™ materials stimulate specific interactions with cells and thereby influence the inflammatory process, wound healing and direct the osteogenic cell differentiation.

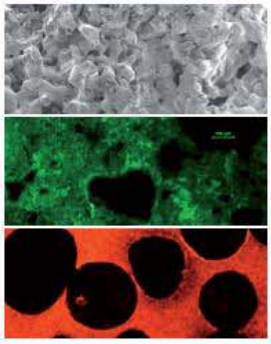


DiaCoating GmbH, Austria

DiaCoating, as a spin-off company of VascuBone, produces and provides novel, functional scaffold material DiaSorb by modification of porous β-TCP scaffolds with nano-diamond particles enabling prompt vascularization to sustain newly formed bone tissue with the following properties:

- Outstanding biocompatibility
- Customized implant geometry and tailor-made surface energy
- Improved hydrophilicity, increase of active surface (up to 100-fold) and stability
- Simple, flexible, stable and efficient technique for immobilization of growth factors (low release, no systemic effects)

Nano-diamond particles are developed and provided by University Würzburg, Chemistry.



PPPolymer AB, Sweden

PPP produces and provides novel polymer scaffold material PPSorb™ with the following properties:

- Synthesis of tin-free PLLA and PCL polymers in large scale, fulfilling cytotoxicity requirement according to DIN ISO 10993-5
- PPSorb™ is resistant to gamma sterilization
- Preparation of 3D scaffolds with different shapes and pore morphology
- A bioresorbable material to be useful as a part of a medical device with vascularization possibilities
- Outstanding biocompatibility
- Enables customized implant geometry with varying pore size distributions

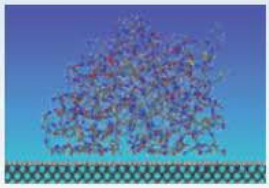
Uppsala Universitet, Chemistry, Sweden

UPPSALA UNIVERSITET

The attachment of various growth factors to diamond and polymer surfaces depends on surface morphology and surface energy. Both of these factors will largely affect the type and strength of attachment between various growth factors and the implant surface.

We calculate:

- Effect of surface morphology on adhesion of growth factors
- Effect of surface chemistry on adhesion of growth factors



Final geometrical structure for Angiopoietin-1 on H-terminated diamond (100)

Toolbox: cell therapies and bioreactor

Tissue Engineering and Regenerative Medicine, Würzburg, Germany

Universitätsklinikum Würzburg

Insufficient nutritional supply due to a lack of blood vessels in the damaged area of critical size bone defects impairs the body's ability to mend fractures appropriately. Therefore, pre-vascularization of bone implants improves the integrative and regenerative potential of tissue engineered bone substitutes.

- Naturally-derived scaffold (BioVaSc®) in combination with synthetic biodegradable biomaterials
- Optimized osteoconductive as well as osteo- and angioinductive properties
- No allogenic factors, thus high immunological acceptance
- Less frequent revision surgeries due to biodegradable properties of the implant
- Regnerative and integrative potential
- Vascularized materials adjustable to medical needs (critical size defects)

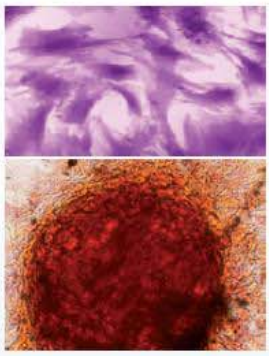
Biomedical Aging Research, University Innsbruck, Austria

universität innsbruck

Mesenchymal Stem Cells (MSC) are residing as a rare population within many body parts and organs. This stem cell type exhibits multipotential differentiation capacities, in particular important for the VascuBone project bringing forth osteogenic precursor cells. To be employed in tissue engineering concepts, primary cells need to be expanded which however may yield replicatively aged cells that are known to perform worse in subsequent applications especially as old cells tend to fall short in osteogenic differentiation.

It is therefore imperative to optimize MSC production processes and quality measures in order to warrant successful tissue engineering of bone as well as the outcome in cell therapeutic applications.

- Enforcing agelessness in cultivated MSC
- Enforcing osteogenic capacity of MSC
- Enforcing attachment and viability of MSC on artificial substrates



EVONIK Industries, Germany

EVONIK INDUSTRIES

Evonik Industries is a worldwide operating specialty company focusing on innovative products and solutions around the megatrends resource efficiency, health & nutrition and globalization. Within Evonik's business line Health care we offer differentiating and valuable products, technologies and services to pharmaceutical, nutrition and medical device companies.

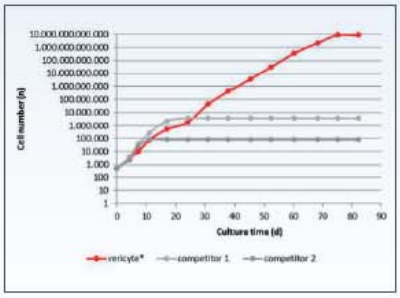
One focus is the development and supply of high quality and GMP conform reagents for the development and optimization of stem cell media which are in line with future regulatory requirements for ATMPs.

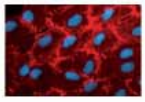
VascuBone – The Partners

Medicyte GmbH, Germany

Medicyte GmbH is a biotech company specializing on the controlled and scalable production of human primary cells. Medicyte´s proprietary technologies upcyte® and vericyte® allow controlled proliferation of primary cells *in vitro*, without loss of phenotypic or cell differentiation properties.

With these unique technologies, the company is ideally positioned to capitalize in the increasing demand for well-characterized primary cell products with consistent quality producible in industrial scales for research and clinical applications.





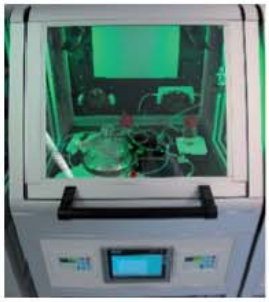
Microvascular endothelial cells cultured in vericyte ® Endothelial Cell Growth Medium are positive for the key markers (here CD31).

Growth of microvascular endothelial cells in vericyte® Endothelial Cell Growth Medium in comparison to growth medium of competitors.

Fraunhofer-Institut für Grenzflächen- und Bioverfahrenstechnik, Stuttgart, Germany

Within the body, cells are responsible for bone regeneration directed by mechanical stimuli such as shear stress and pressure. Several experimental studies have shown that these factors are also inductors for bone generation *in vitro*. We have developed customized bioreactors for the dynamic engineering and *ex vivo* generation of bone grafts.

- Simultaneous application of shear and pressure strain
- Independent regulation of process parameters
- Adaptable to the majority of commercially available roller pump systems



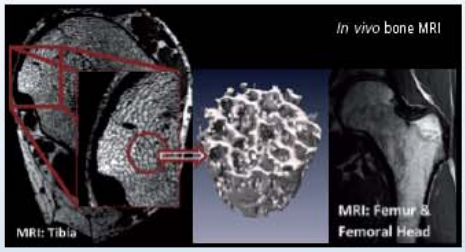
Toolbox: *in vivo* diagnostics – monitoring of regenerative effects with innovative MRI and PET/CT technologies

Diagnostic imaging provides new perspectives to monitor novel regenerative therapies in clinical studies and animal models non-invasively, longitudinally and in real time. In the project framework highly innovative imaging agents and methods specifically tailored for bone imaging have been developed to allow non-invasive characterization of bone implant ingrowth *in vivo*, with regards to various relevant biological processes including cell recruitment, inflammation and vascularization.

MRB Research Center, Germany

The MRB Research Center is dedicated to the development and application of MRI experiments and hardware in all fields of life and material science research, ranging from *in vitro* to *ex vivo* and *in vivo* MRI in pre-clinical animal studies as well as clinical trials in humans:

- High resolution visualization and quantitative characterization of scaffolds for bone regeneration using MRI and microCT
- Detection of cells in biomaterials and monitoring seeding efficiency
- Visualization and characterization of stem cell based bone regeneration *in vivo* in the time course
- High resolution MRI and microCT for quantitative evaluation of therapy results



nanoPET Pharma GmbH, Germany

nanoPET Pharma GmbH focuses on the R&D, production as well as marketing of innovative diagnostic imaging agents. In the VascuBone project, nanoPET Pharma GmbH developed various specialized imaging agents of pharmaceutical quality, which were optimized for use in animals:

- Development of various 1H MRI bloodpool imaging agents (based on Gadolinium and iron oxide nanoparticles) for detection and monitoring of the vascularization of the newly formed bone
- Development of 19F MRI imaging agents for detection of cells in biomaterials and monitoring of seeding efficiency *in vivo*
- Development of various MRI and CT imaging agents for *in vivo* macrophage-assisted inflammation imaging

TOPASS GmbH, Germany

TOPASS is a small sized company in Berlin and a spin-off of the Charité. TOPASS designs and develops nanotechnology products for medical use in diagnosis and therapy. The key R&D activities of TOPASS are related to molecular imaging, regenerative medicine, and diagnostic devices.

Toolbox: pre-clinical and clinical models

Department of Clinical Dentistry, Bergen, Norway
Department for Cranio-, Maxillofacial and Oral Surgery, Innsbruck, Austria

In critical size bone defects after trauma, tumor resection, ischemia or other diseases, autologous microvascular bone transplants are actually the therapy of choice. This can result in donor site morbidity. We developed pre-clincial models for testing an artificially generated bone graft, providing an angiogenic and osteogenic environment with following features and advantages:

- Efficient vascular bed providing vessels for support of large scale bone transplant
- Individual shaping of the bone transplant according to the defect
- Resilient bone grafts for immediate loading
- Avoidance of autologous bone grafting with an additional operation field
- Shorter operation time, as the bone transplant is produced and individualized in advance
- No morbitiy on the autologous bone donor site

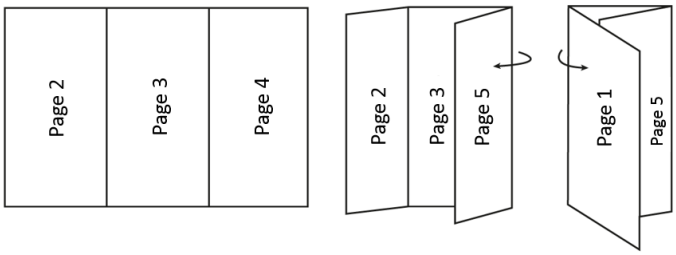
Orthopedic Hospital, Würzburg, Germany

The clinical aim is to revitalize and repopulate the necrotic bone of the femoral head with the injected mesenchymal stem cells, resulting in the regeneration of newly synthesized vascularized bone structure in patients with avascular necrosis (AVN) of the femoral head. The following features and advantages are provided:

- Establishment of logistical and physical prerequisites to conduct "first-in-human" clinical trials
- Establishment of highly effective stem cell therapy strategies for the treatment of musculoskeletal diseases
- Translation of highly innovative stem cell research into clinical application
- Promising therapeutic option for AVN and other musculoskeletal diseases

Additionally a blank template is provided to the partners for creating an insert with their own updated news and results. Thus the Conference Booklet can be disseminated even after VascuBone reporting about current work and collaboration.

The final version will be fold like demonstrated in the next figure:



The print version is shown here:

2 Outlook

The Conference Booklet will be distributed on conferences, workshops, symposia or fairs (see list of planned conferences in Deliverable Report 9.5). In addition the infrastructure and established tools of Fraunhofer Gesellschaft for exhitibions at trade fairs, congresses etc. will be utilized even after the end of VascuBone. This instrument will help to accelerate the transfer of VascuBone results into practice (see e.g. http://www.igb.fraunhofer.de/en/events-tradefairs.html).

Another extensive opportunity to present the Conference Booklet for a broader public will be at the planned lunch symposium at the 4th Conference for Strategies in Tissue Engineering in Wuerzburg, Germany, (10.–12. of June, 2015; www.wite.org) organized by the VascuBone Coordinator.