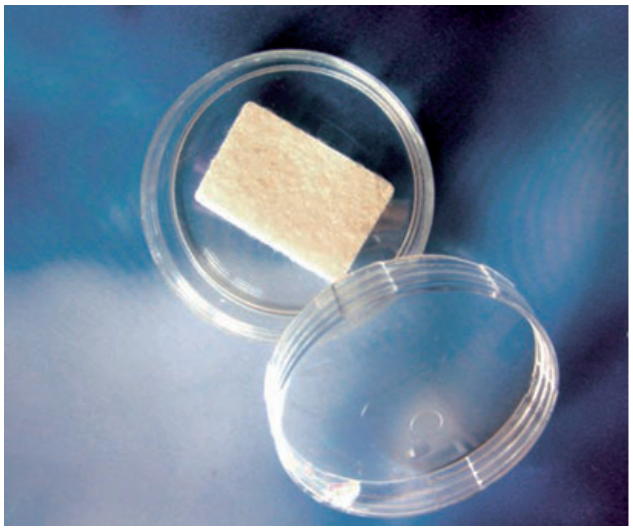
chondrotissue®

THE CARTILAGE IMPLANT
FOR BIOLOGICAL CARTILAGE REPAIR

Content

chondrotissue®

BioTissue is a leading company in the field of biological products for orthopedics. Extensive research and development activities have now brought forth another innovative product for the treatment of cartilage defects.



chondrotissue®

- the cartilage implant

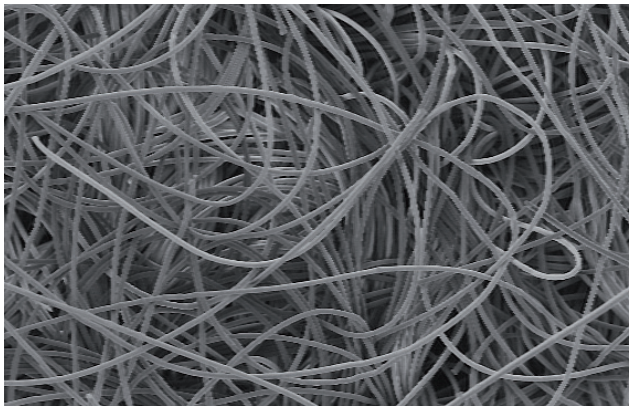
Product Indications :

- chondrotissue® is recommended for use following bone-marrow stimulating techniques such as microfracturing and Pridie drilling
- chondrotissue® is approved for cartilage repair in cases of traumatic and degenerative changes of the synovial joints

Product Features :

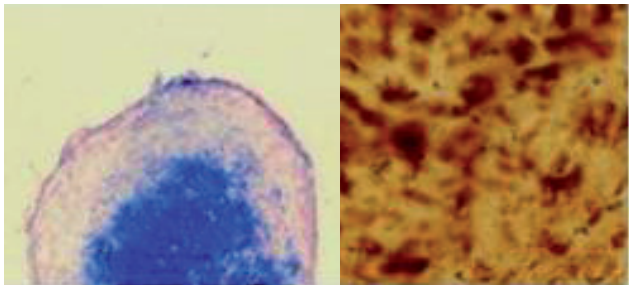
- provides optimal defect covering
- leads to biological defect filling
- induces cartilaginous repair tissue formation
- is approved for use following microfracturing and Pridie drilling
- is used in cases of degenerative and traumatic changes to the synovial joints
- reduces pain and symptoms associated with articular defects
- increases patients' mobility and quality of life

Scientific Background



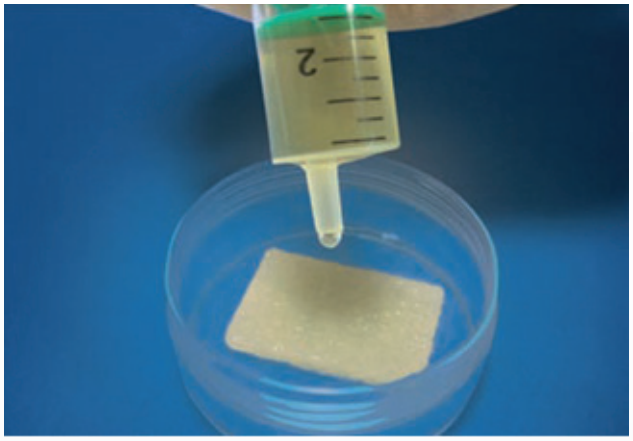
Resorbable polymer-based textile scaffold[6,9]

- guarantees initial mechanical stability
- provides opportunity for stable fixation
- allows optimal, three-dimensional cell distribution
- offers an environment for mesenchymal cells



Hyaluronic acid[6,2]

- is a natural polymer with important functions in the articular cartilage
- provides an important stimulus for chondrogenic differentiation with the formation of hyaline cartilage matrix
- contributes to the viscoelasticity of the cartilage and protects against friction and impact loading



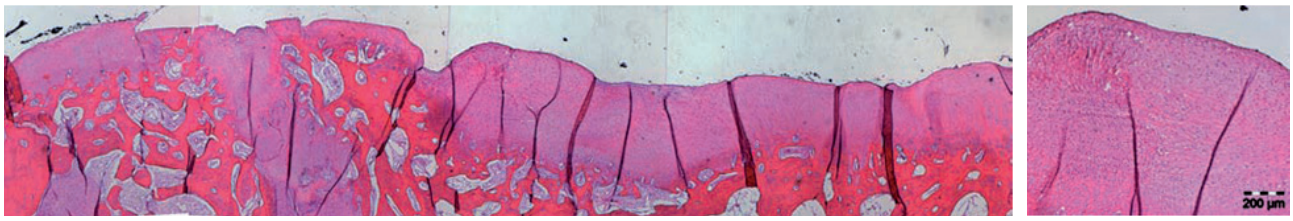
Product combinations[6,9]

- clinically approved in combination with platelet-rich plasma (PRP), human autologous serum and physiological saline for infusion
- human serum stimulates the migration of mesenchymal cells

Preclinical Outcomes

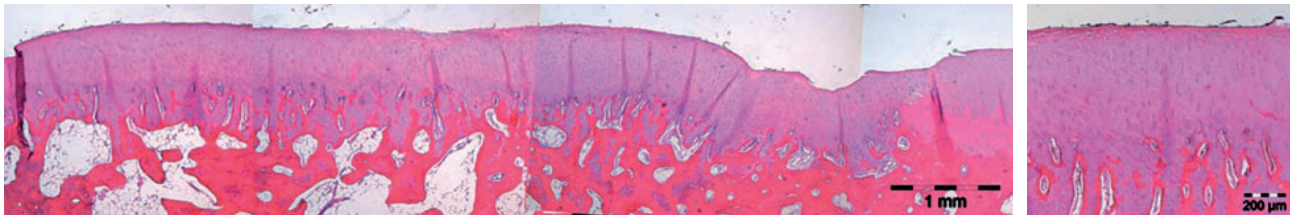
Preclinical studies show that chondrotissue® promotes the formation of cartilaginous repair tissue following microfracturing[6,9]

Microfracturing in the sheep model without defect cover: biopsy after 6 months

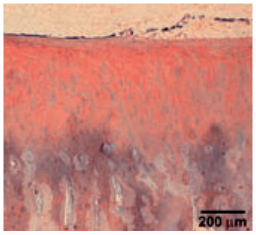


Inferior tissue formation

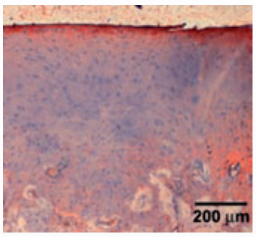
Microfracturing in the sheep model with chondrotissue®: biopsy after 6 months



Hyaline-like tissue



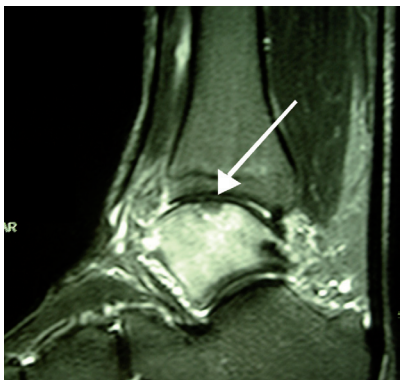
Microfracturing in the sheep model without defect cover: Biopsy after 6 months
Collagen type II staining
- Inferior tissue formation



Microfracturing in the sheep model with chondrotissue®: Biopsy after 6 months
Collagen type II staining
- Hyaline-like tissue

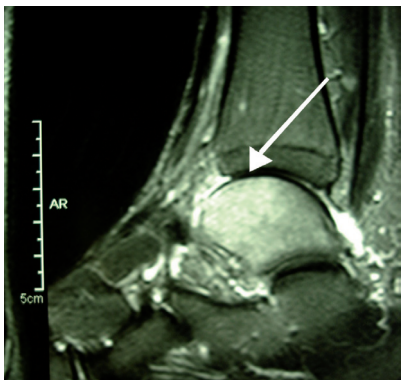
Clinical Outcomes: MRI Evaluation

pre-operative

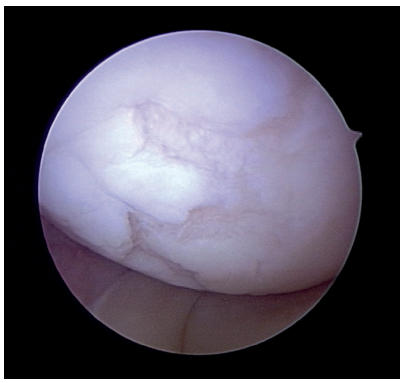


Patient 1: male, 43 years, 0.7cm^2 cartilage defect of the lateral talus[11]

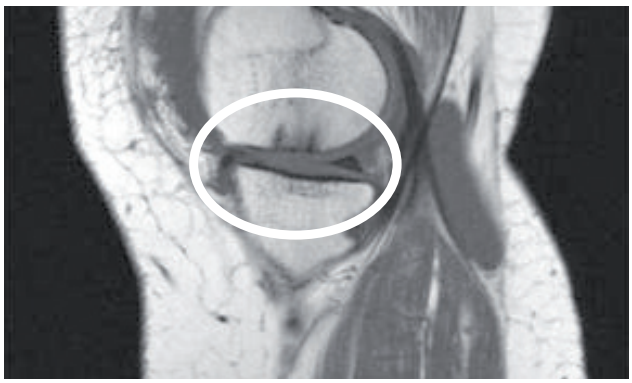
post-operative



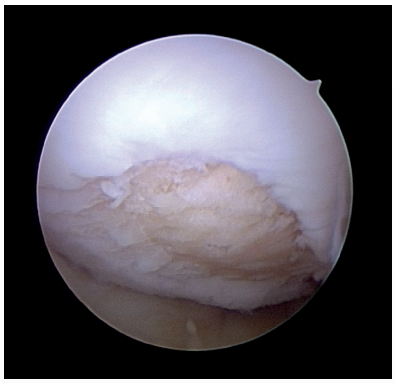
Patient 1: cartilage repair at 7 month follow-up[11]



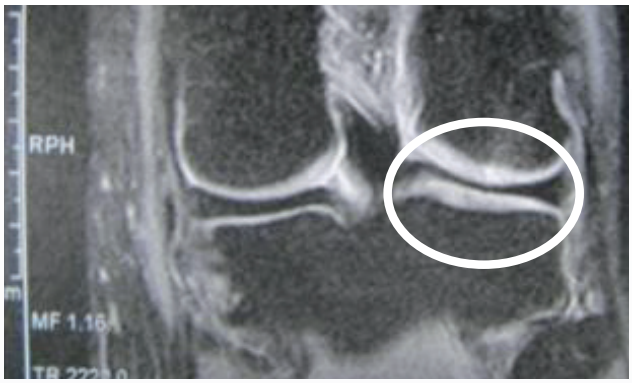
Patient 2: female, 54 years, 3cm^2 degenerative defect of the medial femoral condyle[10]



Patient 2: cartilage repair at 12 month follow-up[10]



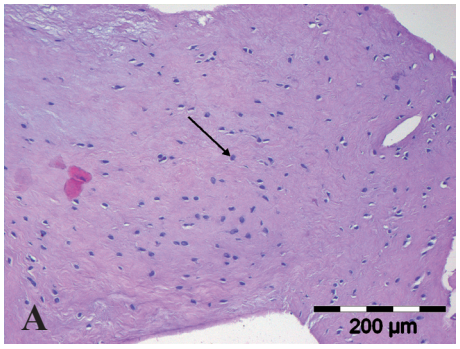
Patient 3: male, 35 years, 4cm^2 traumatic defect of the lateral femoral condyle[10]

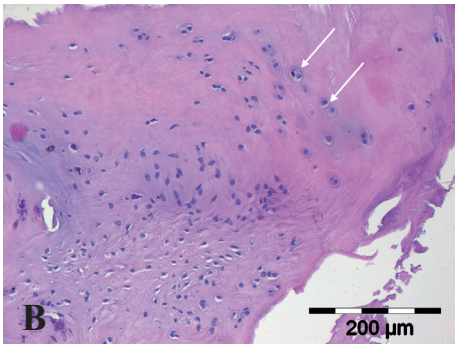


Patient 3: cartilage repair at 12 month follow-up[10]

Clinical data following treatment with chondrotissue® show excellent cartilage repair, high volume defect filling, and smooth peripheral integration of the repair tissue to the adjacent tissue[10,11].

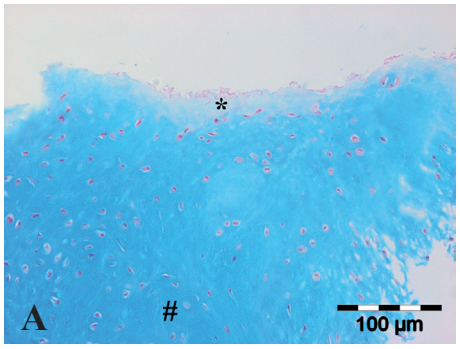
Clinical Outcomes: Histological Evaluation

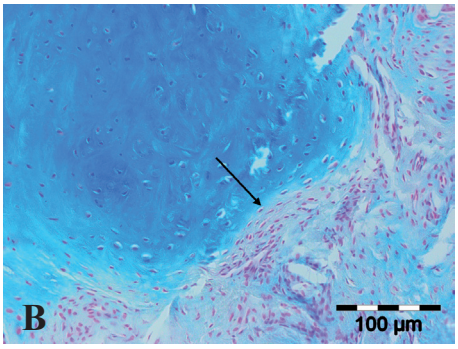




Repair tissue biopsy 18 months after surgery

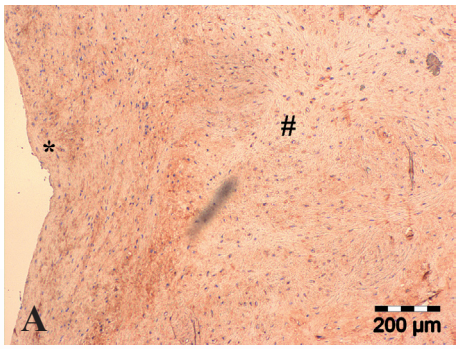
Overview of hematoxylin & eosin staining in biopsy areas with round chondrocytic cells (A black arrow) and cells in a chondron-like formation (B white arrows)[a]

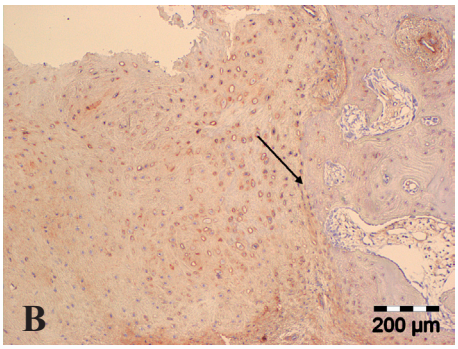




Repair tissue biopsy 5 months after surgery

Positive Alcian blue staining of proteoglycans in a chondro-tissue® biopsy, surface of the repair tissue (A asterisk), central part (A diamond) and bone/cartilage-interface (B black arrow)[b]





Repair tissue biopsy 9 months after surgery

Positive collagen type II staining of a chondrotissue® biopsy, surface of the repair tissue (A asterisk), central part (A diamond) and bone/cartilage-interface (B black arrow)[b]

Histological evaluation shows hyaline-like cartilage tissue, round chondrocytic cells, proteoglycan-rich matrix, and collagen type II formation. The repair tissue is firmly integrated into the subchondral bone and shows a homogenous hyaline-like structure following treatment with chondrotissue®[a,b].

Published with the kind permission of :

[a] Patrascu J.M., MD, Orthopedics and Trauma Clinic II, Victor Babeş University of Medicine and Pharmacy, Timişoara, Romania[13]

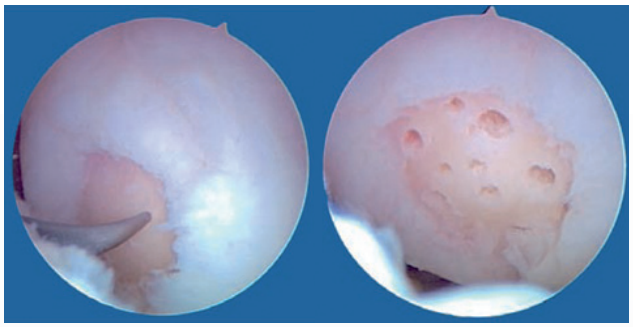
[b] Behrendt S., MD, Evangelic Hospital, Lütgendortmund, Germany (publication in preparation)

Surgery

1 Taking autologous blood samples shortly before arthroscopy

In order to restore the elastic properties of chondrotissue®, it is recommended to mix chondrotissue® with autologous human serum before implantation. For this purpose, approximately 9 ml blood should be drawn from the patient before arthroscopy. The blood should then be centrifuged for 10 minutes or left to stand at room temperature for about 30 minutes until the blood clot has settled. chondrotissue® can also be immersed in human autologous platelet-rich plasma (PRP).

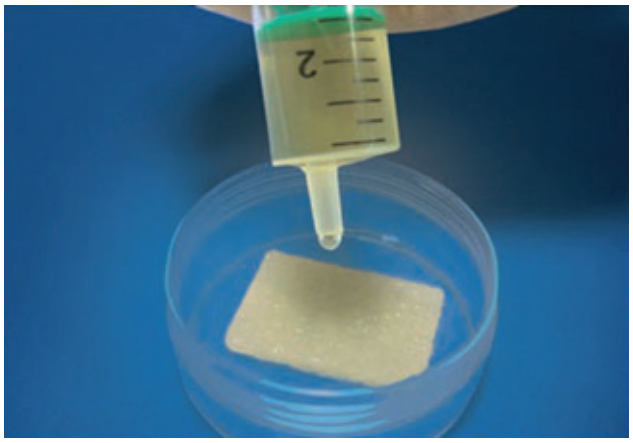
Important: please use serum monovettes, not EDTA monovettes.
If no or too little human serum or PRP is available, physiological saline for infusion can be used or supplemented to reconstitute the elasticity of chondrotissue®.

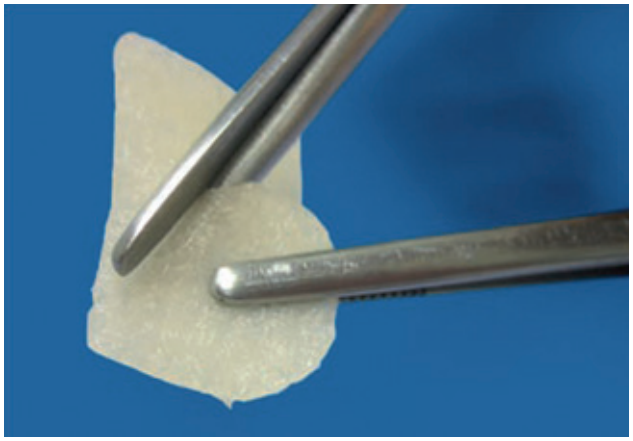


2 Bone-marrow stimulation[1]

Following debridement, the defect should be measured and the subchondral bone perforated with an awl, with spacing of around 3 - 5 mm, during arthroscopy.

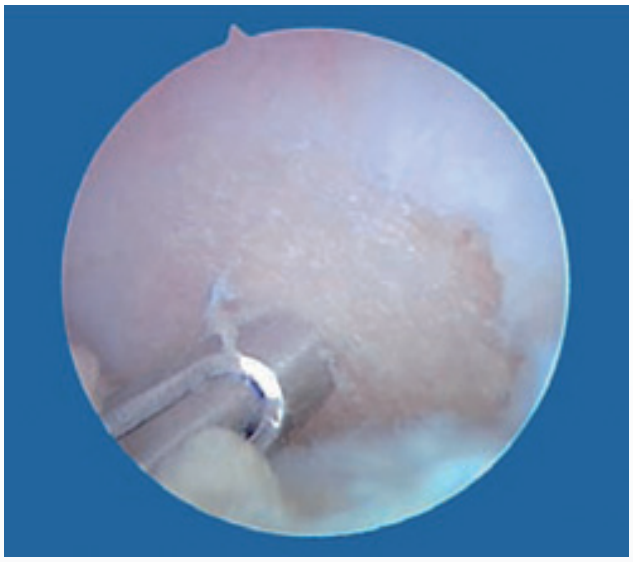
Surgery





3 Preparation of chondrotissue®

Cover chondrotissue® with the patient's own serum, or alternatively with platelet-rich plasma, (2 - 3 ml of fluid are sufficient) and leave to stand for approximately two minutes. This can be done directly in the sterile container supplied. The moistened chondrotissue® can then be cut exactly to size to fit the defect.



4 Fixing chondrotissue®[3,4,7]

chondrotissue® can be fixed in the defect using common orthopaedic fixation methods e.g.:

- **bioresorbable pins**
- **transosseous ancher knot fixation**
- **cartilage suture**
- **fibrin glue** : Please apply the glue to the edges of the chondrotissue® - previously placed in the defect - and distribute it evenly

Please read the package leaflet for more information concerning the product and its use.

Rehabilitation[1]

The information given below is intended only as a recommendation and depends on the size and the site of the defect, the patient's age and the general demands of daily living.

Femoral and tibial defects

	Week 1	Week 2 - 6	After 6 weeks
Loading / Mobilisation	Foot sole contact with walking support / Braces	Foot sole contact with walking support / Femorale condyle – CPM* with restriction Week 2 - 3: 0/0/60° Week 4 - 6: 0/0/90°	Increase of loading to full body weight after two weeks / Free mobility (pain-related restriction)
Walking, sport	Mobilisation	Aqua gymnastics, swimming	Aqua jogging After 8 weeks : cycling After 6 months : jogging After 6 - 12 months : skiing After 18 months : contact sports

Patellar and trochlear defects

	Week 1	Week 2 - 7	After 7 weeks
Mobilisation	Braces	CPM* with restriction : Week 2 - 3 : 0/0/30° Week 4 - 5 : 0/0/60° Week 6 - 7 : 0/0/90°	Increase of loading to full body weight after two weeks / Free mobility (pain-related restriction)
	0 - 14 days	**Weeks 3-4**	**After 4 weeks**
Loading	Foot sole contact with walking support	50% body weight with walking support ; Climbing stairs only with healthy leg	Increase of loading to full body weight after two weeks

* CPM : continuous passive motion

References

1. Steadman et al. Microfracture to treat full-thickness chondral defects: surgical technique, rehabilitation and outcomes. J Knee Surg. 2002.15: 170–6.

2. Hegewald et al. Hyaluronic acid and autologous synovial fluid induce chondrogenic differentiation of equine mesenchymal stem cells: a preliminary study. Tissue and Cell. 2004.36: 431-8.

3. Knecht et al. Mechanical testing of fixation techniques for scaffold-based tissue-engineered grafts. J Biomed Mater Res B Appl Biomater. 2007.83: 50-7.

4. Zelle et al. Arthroscopic Techniques for the Fixation of a Three-Dimensional Scaffold for Autologous Chondrocyte Transplantation: Structural Properties in an In Vitro Model. Arthroscopy. 2007.23: 1073-8.

5. Endres et al. Synovial fluid recruits human mesenchymal progenitors from subchondral spongious bone marrow. J Orthop Res. 2007.25: 1299-307.

6. Erggelet et al. Regeneration of ovine articular cartilage defects by cell-free polymer-based implants. Biomaterials. 2007.28: 5570-80.

7. Petersen et al. Arthroscopic implantation of a three dimensional scaffold for autologous chondrocyte transplantation. Arch Orthop Trauma Surg. 2008.128: 505-8.

8. Neumann et al. Chondrogenic differentiation capacity of human mesenchymal progenitor cells derived from subchondral cortico-spongious bone. J Orthop Res. 2008.26: 1449-56.

9. Erggelet et al. Formation of Cartilage Repair Tissue in Articular Cartilage Defects Pretreated with Microfracture and Covered with Cell-Free Polymer-Based Implants. Journal of Orthopaedic Research. 2009.27: 1353-60.

10. Zantop and Petersen. Arthroscopic implantation of a matrix to cover large chondral defect during microfracture. Arthroscopy. 2009.25: 1354-60.

11. Bergmann and Abt. Case Report: 7 months clinical follow-up after arthrotomic implantation of chondrotissue® in a cartilage lesion of the lateral talus. Fuß & Sprunggelenk.2009. doi:10.1016/j.fuspru.2008.11.013

12. Kalwitz et al. Chemokine Profile of Human Serum from Whole Blood: Migratory Effects of CXCL-10 and CXCL-11 on Human Mesenchymal Stem Cells. Connect Tissue Res. 2010.51: 113-22.

13. Patrascu et al. Repair of a posttraumatic cartilage defect with a novel cell-free polymer-based cartilage implant: A case report with 2 years follow-up by magnet resonance imaging and histology. J Bone Joint Surg Br, in press.

References

Further publications about scaffold-based cartilage regeneration:

Sittinger et al. Engineering of cartilage tissue using bioresorbable polymer carriers in perfusion culture. Biomaterials. 1994.15: 451-6.

Sittinger et al. Resorbable polyesters in cartilage engineering: affinity and biocompatibility of polymer fiber structures to chondrocytes. J Biomed Mater Res. 1996.33: 57-63.

Sittinger et al. Tissue engineering and autologous transplant formation: practical approaches with resorbable biomaterials and new cell culture techniques. Biomaterials. 1996 .17: 237-42.

Rotter et al. Behavior of tissue-engineered human cartilage after transplantation into nude mice. J Mater Sci Mater Med. 1999.10: 689-93.

Perka et al. Chondrocyte transplantation in PGLA/polydioxanone fleece. Orthopäde. 2000.29: 112-9.

Perka et al. Tissue engineered cartilage repair using cryopreserved and noncryopreserved chondrocytes. Clin Orthop Relat Res. 2000.378: 245-54.

Duda et al. Mechanical quality of tissue engineered cartilage: results after 6 and 12 weeks in vivo. J Biomed Mater Res. 2000.53: 673-7.

Kaps et al. Molecular characterization of tissue-engineered articular chondrocyte transplants based on resorbable polymer fleece. Orthopäde. 2004.33: 76-85.

Barnewitz et al. Treatment of articular cartilage defects in horses with polymer-based cartilage tissue engineering grafts. Biomaterials. 2006.27: 2882-9.

Kaps et al. Gene expression profiling of human articular cartilage grafts generated by tissue engineering. Biomaterials. 2006.27: 3617-30.

Ossendorf et al. Treatment of posttraumatic and focal osteoarthritic cartilage defects of the knee with autologous polymer-based three-dimensional chondrocyte grafts: 2-year clinical results. Arthritis Res Ther. 2007.9: R41.

Endres et al. Human polymer-based cartilage grafts for the regeneration of articular cartilage defects. Tissue Cell. 2007.39: 293-301.

Kreuz et al. Treatment of focal degenerative cartilage defects with polymer-based autologous chondrocyte grafts: four year clinical results. Arthritis Res Ther. 2009.11: R33

BioTissue AG

Scheideggstrasse 73
CH-8038 Zürich

phone : +41 (43) 222 40 04
fax : +41 (43) 222 40 02
customerservice@biotissue.ch
www.biotissue.ch