

LADDEC® Clinical Overview



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Effects of Laddec on the formation of calcified bone matrix in rat calvariae cells culture.

S Hofman, M Sidqui, D Abensur, P Valentini, P Missika. Biomaterials. 1999;20(13):1155-1166.

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Osteoblasts from 21 day-old fetal rats calvaria were isolated using a collagenase digestion procedure. Cells were cultured in the presence of Laddec (a highly purified bovine xenograft) and Bio-Oss (natural bone mineral). Optical microscopic observations showed that osteoblasts attached on the plastic culture dishes and formed close contact with biomaterial particles. By day 5, the osteoblasts formed a confluent monolayer. A cytozymatic method showed intense alkaline phosphatase (ALP) staining around and between the substrate granules of the two materials. By day 14, inverted phase microscopic observations showed that osteoblasts formed bone nodules around and between substrate particles. In addition, at this time, the Von Kossa staining was positive. Using a conventional assay, ALP specific activity was higher in the presence of Laddec than in the presence of Bio-Oss. A quantitative morphological method using image analysis showed that the proportion of mineralized bone formed around biomaterial particles in relation to total bone was increased with Laddec (15% more than with Bio-Oss). Ultrastructural observations by TEM showed the presence of an electron dense collagen-free layer at the biomaterial/bone interface and a collagenous matrix deposited at the periphery, indicating the bioactivity of the biomaterials. These results indicated that Laddec increased the expression of ALP in osteoblast cultures and facilitated the formation of multiple cell layers, providing a culture environment suitable for mineralization.

Bone graft substitutes: a comparative qualitative histologic review of current osteoconductive grafting materials.

KA Ruhaimi. Int J Oral Maxillofac Implants. 2001;16(1):104-114.

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This paper investigated the osteogenic potential of 6 osteoconductive grafting materials derived from human, bovine, and synthetic sources: HTR, BOP, Biogran, Laddec, Dembone, and Osteograf. Twenty-eight New Zealand rabbits were used in this study. The active group consisted of 24 animals and the control group consisted of 4 animals. The median condyle of each tibia was drilled with a 5-mm-diameter bur to form 8 mm-deep cavities. A control group included 8 osseous cavities, with 1 hole in each tibia. These cavities were washed and left unfilled. In the active group, each grafting material filled 8 osseous cavities in 8 tibiae of different animals. Half of the active and control osseous cavities were investigated with decalcified hematoxylin and eosin-stained sections. The other half were studied with scanning electron microscopy. It was concluded that Laddec bovine bone granules possessed the best potential for an osteoconductive grafting material, followed by the bioglass crystals of Biogran and the hydroxyapatite particles of Osteograf, respectively. The least potential for rapid bone formation was demonstrated by the copolymers of HTR and BOP, and Dembone allograft bone particles did not reveal active bone healing.



Biomaterials for bone filling: comparisons between autograft, hydroxyapatite and one highly purified bovine xenograft.

*D Chappard, A Zhioua, F Grizon, MF Basle, A Rebel.
Bull Assoc Anat (Nancy). 1993;77(239):59-65.*

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Bone grafts are becoming increasingly common in orthopaedics, neurosurgery and periodontology. Twenty one New Zealand rabbits were used in the present study comparing several materials usable as bone substitutes. A 4.5 mm hole was drilled in the inner femoral condyles. Holes were filled with either an autograft (from the opposite condyle), an hydroxylapatite (Bioapatite), or a highly purified bovine xenograft (T650 Lubdoc). Animals were sacrificed at 1, 3 and 6 months post implantation and a quantitative analysis of newly-formed bone volume (BNF/IV) and remaining biomaterials (BMAT/IV) was done. In addition, some holes were left unfilled and served as controls. At 6 months, there was no tendency for spontaneous repair in the control animals. The autografted animals have repaired their trabecular mass and architecture within the first month. Hydroxylapatite appeared unresorbed at six months and only thin and scanty new trabeculae were observed. The xenograft induced woven bone trabeculae formation on the first month. This was associated with resorption of the material by two multinucleated cell populations. At six months, the epiphyseal architecture was restored and the biomaterial has disappeared in most cases. Xenografts appear a promising alternative to autografts and allografts, whose infectious risks and ethical problems should always be borne in mind.

Comparison of mechanical properties of human, bovine bone and a new processed bone xenograft.

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Biomaterials. 1993;14(5):337-340.*

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The study compared the mechanical properties of human bone, fresh bovine bone and a new highly purified bone xenograft: T650 (Lubdoc-Laddec). Destructive, compressive tests were performed to determine Young's modulus and ultimate strength, with a constant deformation rate of 0.025 mm min⁻¹. The stress-strain curves obtained from all the non-human specimens especially the T650, did not differ significantly from those observed with human bone. Human and fresh bovine samples presented a significantly different Young's modulus. The T650 samples, depending upon their trabecular texture (dense or medium) also differed significantly from each other (132.9 +/- 52.3 versus 80.0 +/- 37.3 MPa, P < 0.05). Their moduli were similar to those of bovine and human cancellous bone, respectively (117.49 +/- 61.53 versus 77.36 +/- 54.96. P < 0.05). The ultimate strength of T650 dense (9.6 +/- 3.7 MPa) was similar to bovine (8.5 +/- 4.2 MPa) and human bone (8.78 +/- 5.2 MPa); the T650 medium (5.9 +/- 2.8 MPa) was significantly different from the other specimens.



Bovine heterologous bone graft in orbital surgery.

S Morax, T Hurbli, R Smida.

Ann Chir Plast Esthet. 1993;38(4):445-450.

Service d'Ophtalmologie, Fondation Ophtalmologique A. de Rothschild, Paris.

Lubboc (T650) is a bovine heterologous bone implant obtained by specific preparation of trabecular of bone. In vitro and in vivo biocompatibility studies have revealed the absence of any cytotoxicity or systemic toxicity. Lubboc has many fields of application, including all bone graft surgical indications. We report our first results concerning the use of this product in orbital surgery either as a filling or contention material or as an apposition material. On all 20 operated patients we did not encounter any intolerance, inflammation or infection. The follow-up is still too short to appreciate the long term integration of this material which has the advantage of being a substitute for autologous bone, avoiding bone graft harvesting.

Type I collagen in xenogenic bone material regulates attachment and spreading of osteoblasts over the beta1 integrin subunit.

MF Baslé, M Lesourd, F Grizon, C Pascaretti, D Chappard

Orthopade. 1998;27(2):136-142.

Laboratoire d'Histologie-Embryologie, Faculté de Médecine & CHU Angers (LHEA).

Xenogenic bone biomaterials have been proposed as an alternative to autografts or allografts in human bone restoring or in complement of prosthetic surgery. When appropriate treatments were applied, immunological, inflammatory, bacteriological or virological adverse responses can be prevented. However, these treatments may interact with type I collagen, the major component of the organic bone matrix. Type I collagen can bind osteoblasts via specific cell surface receptors, the integrins. In this work, two different xenogenic biomaterials were studied. Both biomaterials have a bovine bone origin. They displayed similar architectural organization with connected plates and rods and similar surface topography and roughness. They differed by the presence or not of collagen type I. The first one was characterized by preservation of the type I collagen matrix associated with spindle-shaped hydroxyapatite crystals and the second was solely composed by heat-modified apatite crystals. Osteoblast-like cells (Saos-2) were cultured on both biomaterials and examined in scanning and transmission electron microscopy after 7 and 14 days. Both biomaterials were cytocompatible as demonstrated by good ultrastructural cell preservation. (1) At the surface of the collagen containing biomaterial, cells were elongated in shape and oriented according to the trabecular architecture and to the superficial collagen network. After 14 days of culture, cells were confluent and the biomaterial surface was hidden by the cell sheet. The beta 1 integrin subunit was detected by immunogold in transmission electron microscopy in close relationship with the superficial collagen fibres of the biomaterial and with the outer cell surface. When cultures were carried out in presence of anti beta 1 integrin subunit, cells were packed and piled up with lack of specific orientation. (2) At the surface of the deproteinized biomaterial, cells were globular without specific disposition and often partially attached to the surface. After 14 days of culture, large areas of the biomaterial surface remained uncovered. Anti beta 1 subunits conjugated with gold particles were detected around the cells but with no specific association with the deproteinized biomaterial. These results strongly suggest that presence of type I collagen fibres in the matrix of a bone biomaterial is of major interest to determine cell attachment, spreading and orientation via interaction between type I collagen and beta 1 integrin subunit of osteoblasts.



Shape and orientation of osteoblast-like cells (Saos-2) are influenced by collagen fibers in xenogenic bone biomaterial.

MF Baslé, F Grizon, C Pascaretti, M Lesourd, D Chappard.
J Biomed Mater Res. 1998;40(3)350-357.

Laboratoire d'Histologie-Embryologie, Faculté de Médecine, Angers, France.

The surface topography of a substratum has been shown to influence the growth and morphology of cells in culture. In this study, human osteoblast-like cells (Saos-2) were cultured on two types of xenogenic biomaterials obtained from bovine bone. Both biomaterials were similar in architectural organization and surface topography, but they differed in matrix components. The first one was characterized by preservation of the mineralized collagen matrix, and the second by complete deproteinization which only preserved the mineral phase. Cells cultured at the surface of both biomaterials were observed using scanning electron microscopy. The beta 1-integrin subunit, known to bind cell and collagen, is the major integrin of the osteoblast. It was localized using immunogold in transmission electron microscopy. At the surface of the collagen-containing matrix, cells exhibited an elongated shape and oriented axis parallel to the underlying collagen bundles. The beta 1-integrin subunit was localized at the outer surface of cells, in close association with collagen and at the contact points between cells and biomaterials. In contrast, at the surface of the single mineral matrix, cells were round shaped with random disposition. Gold particles were found around the cells with no specific relation to the biomaterial. These results strongly suggest that the chemical nature of the surface of a bone biomaterial directly influences adhesion process, shape, and spatial organization of cultured osteoblastic cells.



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