Dr. Lajos Gáspár

Experiences in the application of

**BONEALBUMIN HUMAN ALLOGRAFT**

The Author hereby expresses his special thanks to Dr. Csák Csaba, Dr. Glasz Tibor, Dr. Harváthy Dénes, Dr. Lacza Zsombor, Dr. Simonffy László, Dr. Trimmel Bálint, Kónya János, Dr. Kivovics Márton, Prof Dr. Szabó György, Dr. Csongé Lajos, Dr. Török Roland, Dr. Tóka József, Dr. Benedek Gábor, és Dr. Szabó Zoltán, whose works and performances contributed to the expansion of our knowledge in the experiences in the examination and application of BoneAlbumin.

In significant part of bone shaping processes, interventions of implantology and oral surgery are supplemented by the substitution of the amount of bone necessary for the ideal or minimal amount. For the substitution of bone losses, there are several different materials of human or animal origin, as well as synthetic materials. Initially, based on the wide range of literature in this topic, we can determine that none of the today applied methods, materials or procedures are perfect.

### States of bone losses

Following the loss of teeth and resorption of the bone, bone supply may be so poor, as:

- **Implant cannot be possible to put in a traditional way**—according to Misch—when the horizontal width of the alveolar crest is smaller than 5 mm, or vertical height is smaller than 8 mm.
- **Even if implant can be put, there is such a thin bone layer around the implant, that the success of ossification is not sure.**
- **Primer stability cannot be accessed.**
- **A certain part of the side surface of the implant is not covered by bone.**
- **A certain part of the implant in not under bone level.**

In states of bone losses, before putting implants, possibilities for treatments can be divided into 4 groups:

1. **Bone—rendered suitable by bone shaping**
   Plastic transformation of the available alveolar crest in order to make it able to admit the implant
   - **Horizontal expansion**—widening
   - **Vertical expansion**—raising
   - **Condensation**—to access the appropriate bone density

2. **Into bone rendered suitable by bone grafting:**
   - **Autograft** - The graft originates from the same person.
   - **Allograft** - The donor and the recipient entities belong to the same species, but genetically they are not identical.
   - **Xenograft** - The graft originates from different species than it will be put in.
   - **Synthetic materials** - Hydroxiapatite, bio ceramics, beta tricalcium phosphate, calcium sulphate.

3. **Into bone rendered suitable by bone shaping and bone grafting:**
   - Surgical technique of bone grafting Lateral augmentation, sinus lifting, bone splitting.
   - Bone grafting materials, according to their origin: autograft, allograft, xenograft, synthetic materials
   - Bone grafting devices.

4. **Into bone rendered suitable by guided bone regeneration (GBR) technique:**
   - Nonabsorbable diaphragms -Teflon Gore tex, Titan reinforcement PTFE (polytetrafluoro-ethylene)
   - Absorbable diaphragms - collagen, /BioGuide (4–6 months), polylactic acid (PLA), poliglycolic acid (PGA), EpiGuide (6-12 months), liophilised dura mater, Lyodura, Lyoplant.

Because of the fear from bovine spongiform encephalopathy (BSE), nowadays, the use of the otherwise popular bovine has significantly decreased, while in the recent years, the interest in synthetic or allograft materials has showed a significant increase.

### Synthetic bone grafts

One of the popular synthetic materials is the pure phase β tricalcium phosphate (β-TCP). Based on both animal experiments and clinical results, its advantage is that neither of the material itself, nor its degradation product is toxic, it cannot contain viruses, prion or any other protein. It is tissue friendly, its remodelling does not result in inflammatory symptoms. The clean β tricalcium phosphate (β-TCP), as a Cerasorb, is also a widely used osseoconductive material. Due to its chemical features, while the osteosorption its resorption is quick and complete.
While its introduction, platelet rich plasma, (PRP) raised high hopes, which, due to its factors, improves ossification. But until now, we haven’t found such literature, where data would prove the significantly beneficial combined effect of PRP and synthetic bone grafts—rather, on the contrary, in fact.

Bone grafts of xenograft are mainly of bio materials of bovin origin, which consists of calcified matrix. One of them, called Bio-Oss is an efficient xenograft which can be used safe—it is a bone derivative of deproteinized and sterilized bovin with 75-80% porosity. It has outstanding osseoductive features.

Calcium phosphate cement (CPC, e.g. VitalOs) solidifies very quickly, crosslinking around the formation of the new bone.

The most important features of bone grafts

The use of today’s new bone grafts allows that contrary to spontaneous recovery, the regeneration shouldn’t be scarring or connective tissue remodelling, which contain the formation of—from the aspect of implantology—valueless tissues. The material which is to be put in should meet several requirements. It shouldn’t damage the implant receiver organism, it shouldn’t contain any infectious agent, thus it shouldn’t transmit any infections. If it is possible, bone resorption should be continuous and synchronized with osteogenesis, giving way to the forming new bone tissue gradually. The principle of remodelling should be prevailed: the new bone should be similar to the original one, moreover, it shouldn’t delay but has a positive, osseinductive influence on the ossification process, and it shouldn’t improve formation of bone at places where originally—e.g. outside of periosteum—there wasn’t any.

Application of own bone is known in several bone grafting methods, and for more than 50 years it is applied with success; however, there is a growing demand on other type of bone grafting materials, as well. Beef bone, which had been prevalent and successfully applied for decades, seems to be excluded from the practice, while professional attention turned towards other materials and new solutions.

Bone grafting materials

For bone grafting—as we know it very well—there can be several materials applied. Here we can’t afford to review the complete list of them, but we can highlight the most typical ones introducing their features, as well. While the choosing, process the advantages and disadvantages of the available materials shall be considered. All over the world, autologous bone grafts are still the gold standard. From the aspect of biocompatibility, it is optimal. Although, its disadvantage is that it has limited availability, while in all cases it needs a second surgical intervention.

In oral surgery and implantology it is particularly critical, as bone grafting is necessary in those cases and patients where there is not enough bone available. Thus, bone taking which is necessary for bone transplant is limited.

While smaller augmentations where own bones are used, the available amount of autologous bone can be obtained from intraoral surgical intervention as well, but for frequently applied sinus elevation or bone demand of greater volume, autologous bone can be obtained from the iliac crest, by bone transplant. However, this operation is quite a serious one. The question arises, whether the second surgical intervention is proportionate to the target of the original operation, therefore, the augmentation. It must be considered that the second surgical intervention increases the risk of the operation, and in most cases, in the donor region there is a stronger, longer lasting pain, moreover, there are more complications happened than while the first intervention.

Knowing these, several professionals pointed out the necessity of autologous bone grafting in the 1980s. There were countries, where the application of allogeic bone transplant was a widely-spread method, while in others—due to legislative obstacles—it remained limited. The great advantage of this method is that there is no need for a second surgical intervention. However, there is the danger that due to its not diagnosed disease, the donor may transmit infections. Furthermore, rejection reaction may also be possible—as in all cases of transplanted tissues. It is true for the materials of the otherwise popular bovin origin, as well.

The above risks may be prevented by the application of synthetic materials, which become more and more perfect and popular, while they are available without limits and second surgical intervention. Disadvantage of them is not to have any osseoductive features. Regarding their chemical and physical features, the different known synthetic materials differ from each other.

For the classification of alloplastic materials, resorption tendency, phase-purity, solidity and porosity are important criteria.

Resorption tendency is one of the basic requirements for real regeneration, therefore, the ideal outcome of the treatment. Formation of new bone simultaneously with the complete resorption of the bone graft can lead to the reparation of the original conditions, exclusively. Phase-purity guarantees homogeneity and same absorbency, which provides continuously solid augmentation under the resorption, as well. We know that foreign phases are absorbed in a slower manner, or they do are not absorbed at all—remaining in the new bone tissue forming small islands there. While the remodelling process, these remaining islands obstruct the formation of bone trabeculae appropriate to the direction of loading. So as to avoid the early resorption of the augmentation put in, thus the unsuccessful process, initial solidity is necessary, which ensures constant volume under the
It is an important issue that the rate of proliferation of stem cells is improved by both growth factors. However, as we can see, they do not result either in the faster resorption of the augmentation, or in the delay of the formation of new bone. It has been proven that the positive effect of PRP results in the faster transformation of the new bone into a lamellar bone, which provides the appropriate bone density and quality sooner—which is essential from the aspect of the stability of the implant.

In the last years, the application of natural and synthetic calcium phosphate ceramics appeared in bone grafting as a significant alternative solution. Regarding their mineral composition, features and micro architecture, these materials are quite similar to human trabecular bone, while they show high affinity for proteins.

According to their chemical composition, calcium phosphate materials—applied in practice—can be hydroxyapatites (HA), beta tricalcium phosphates (β-TCP), the combination of biphasic calcium phosphates and beta tricalcium phosphates (combination of HA and β-TCP), and carbonate-free apatite. At the same time, literature contains such modification processes, according to which a change in the content of the materials results in a significant change of the biological features of the whole material. One of these successful modification processes is the substitution of phosphate with silicate ion (Si-CaP), which resulted in a material with new features, which proved to be useful in the process of bone formation.

Today, with the rapid development of dental implantology it has been clear that the most important requirement against bone grafting is the permanent result which lasts for years and the remodelling of the bone grafting material. Thus, it is a clear basic requirement against bone grafting materials, that the human body should not give immune response for them, and its application should cause as small operational load on the patient as possible. It is also very important that the application of them should remain within the limits of costs.

**BoneAlbumin**

Regarding their features, all the traditional allografts, xenografts and synthetic materials are less valuable than own bone, this is why both tendencies (own and not own bone) have advantages and disadvantages.

The advantages of these tendencies mentioned, are combined in a new method, where from a bone taken out of alive and otherwise examined human by an orthopedic operation experts create an alloplastic material, which— following appropriate processes—they treat with albumin. The created material, called BoneAlbumin, has become a part of the toolbox of dental implantology with features significantly different from previous materials (Skaliczki G et al. – 2013, Klára T et al. – 2014, Horváthy D et al. – 2016, Schandi K et al. – 2016).
Animal experiments

Since 2006, under the leadership of dr. Lacza Zsombor, the Hungarian working teams have been working on this new method within the framework of BoneAlbumin researches. The examination of the material had been started by animal experiments, then, after receiving the necessary authorizations, experts made the first human implants. Based on the positive laboratory, clinical and histological results they made further developments. The dental, oral surgery and clinical examinations regarding its human application started in 2015.

When implanting hip prosthesis, while the operation the femur head as a living bone will be released and from this bone ball with the diameter of 5cm it will be possible to produce—with the method worked out by the mentioned working team—a kind of granules, a bone block. For its use in oral surgery, dentistry and implantology, the necessary authorizations are available, the clinical examination programs have been started, and the first results have already been received.

As a result of animal experiments, it has been proven, that BoneAlbumin:
1. is an active substance;
2. accelerates ossification;
3. provides a surface suitable for the adhesion of progenitor cells
4. decreases the colonization of bacteria

Tissue bank

The experts of the West Hungarian Regional Tissue Bank of the County Hospital in Győr, under the leadership of dr. Csöngé Lajos, by bone physiological and bone histological examinations and methods, have studied the features and behavior of human allograft treated with albumin as well as the most important steps of the formation of types of bone allograft materials. According to their opinion, ideal bone donor is not older than 40 years, and for the formation spongiosa or corticospongiosa parts are necessary. The grain size in the bone granules may vary, it may be smaller than 0.5mm or around 2mm or even bigger than that. And bone blocks can be formed in a pre-set size. According to the Urist protocol, while the formation of bone graft, bones of human preparation should be first, desantigenised, then partly decalcinated, and finally, lead through self-digestion (autolysis) and chemical sterilisation. Next, there is albumin added to the preparation. The osseoconductive, osseoinductive and osteogenesis-inductive effects of BoneAlbumin improve the build-in process of bone graft.

Clinical application

While the 3D-planning and the work out of the first steps and methods of the individual bone block in the dental laboratory (dr. Csák Csaba, Könya János, dr. Tóka József), first, based on the CT-image of the patient, the planning starts with the determination of dimensions. Then, with the help of a computer-controlled program, according to the individual bone loss of the patient, the bone block will be formed. The steps of the virtual planning are followed by CAD-CAM bone shaping, when from the bone block, the individual, precise 3-dimension block will be shaped.

While the implant of 3D-planned, and -formed bone blocks, on the ready block is not required to do any corrections, because it can be put in almost immediately. The intercourse through a wide surface accelerates and makes the vascularization and building-in of the block even safer. Grafting is not necessary to be supplemented by granules, and the operation is safer and faster, than in the cases when the bone block is from the patient’s own bone. Although, wound closure by a tension free lobe has a major importance. The operation should happen under antibiotic protection and it is important not to make BoneAlbumin wet, it can be put on the surface immediately and directly, without any pre-treatment. So as to avoid the loading of the block above the implanted bone it is not advised to use any prosthesis, and the patient should avoid smoking for at least 3 weeks.

Experts have compared the behavior of bovin Bio-Oss to human BoneAlbumin, at socket preservation following the extraction of lower wisdom-teeth. The examined demarcation, postoperative pain and oedema, as well as the success of the healing process of the bone. For BoneAlbumin, experts had positive experiences.

There have been clinical working teams to examine the effects of BoneAlbumin, in the area of socket preservation following extraction of wisdom-teeth (dr. Simonffy László, dr. Gyulai Gaál Szabolcs, dr. Trimmel Bálint), in the cases of sinus lifts (prof. dr. Szabó György, dr. Kivovics Márton), and, in the clinical implant practice (dr. Benedek Gábor, dr. Tálos Mariann), which results have been published in several professional forums.
BoneAlbumin application in the Gáspár Medical Center

In the Gáspár Medical Center, experts examined primarily the combined application of BoneAlbumin and magnetic hammer. In the framework of that, there were socket preservation, bone splitting, lateral and vertical bone augmentation, rehabilitation of chin defects following cystectomy, as well as sinus-lifts got into the test groups.

Between 1 October, 2014 and 1 April 2017, we applied magnetic hammer for 419 patients.

<table>
<thead>
<tr>
<th>Type of intervention</th>
<th>Male (pers.)</th>
<th>Female (pers.)</th>
<th>Total (pers.)</th>
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<tbody>
<tr>
<td>Tooth extraction and/or immediate implantation</td>
<td>37</td>
<td>55</td>
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<tr>
<td>Bone compression</td>
<td>39</td>
<td>73</td>
<td>112</td>
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<tr>
<td>Horizontal bone expansion</td>
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<td>65</td>
<td>124</td>
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<tr>
<td>Vertical bone expansion</td>
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<td>40</td>
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<tr>
<td>Sinus lifting</td>
<td>14</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td>Cyst bone graft</td>
<td>8</td>
<td>13</td>
<td>21</td>
</tr>
<tr>
<td>Összeesen</td>
<td>176</td>
<td>244</td>
<td>419</td>
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Between 1 March, 2015 and 1 April 2017, we applied the combination of magnetic hammer and BoneAlbumin for 102 patients.

<table>
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<th>Female (pers.)</th>
<th>Total (pers.)</th>
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<tr>
<td>Tooth extraction and/or immediate implantation</td>
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<tr>
<td>Bone compression</td>
<td>11</td>
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<td>6</td>
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<tr>
<td>Sinus lifting</td>
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<td>11</td>
<td>21</td>
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<tr>
<td>Cyst bone graft</td>
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<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>56</td>
<td>102</td>
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For cases of implantation assisted by magnetic hammer, there were 835 implants put in.

<table>
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<th>Number of patients (pers.)</th>
<th>Number of implants (pcs)</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>155</td>
</tr>
<tr>
<td>Female</td>
<td>247</td>
</tr>
<tr>
<td>Total</td>
<td>402</td>
</tr>
</tbody>
</table>

Among implants put in, there were 81 pieces of MIS, 103 pieces of Straumann, 565 pieces of SGS, 72 pieces of Pat-top, 11 pieces of Bego Semados and 3 pieces of Denti got into the program.

Case studies

Case 1 (abb 2)
For P.I. 58-year-old female patient in subtotal upper jaw tooth loss, we made sinus lift on the right side, we applied BoneAlbumin (granules) as a bone grafting material. The splitting of the quite thin alveolar process was made...
by bone cutting blade of magnetic hammer. At the end of the ridge, we split the knife-edged ridges of 2—4 mm vertically, grafted it with BoneAlbumin chips, widened it and covered with a diaphragm. At the end of the ridge, we augmented the extremely thin ridge of 2—3 mm to the width of at least 5.5 mm. Panoramic radiography and CT images show the significant amount of bone grafting. Following the bone grafting process, the wound healing was untroubled.

While the second operation, 6 months after the bone grafting process, with the help of a magnetic hammer, without drilling we put in 7 implants to the upper jaw.

While the operation with the help of a bone trepan—as the first step of the formation of the implant bed—we made bone biopsy from the upper alveolar crest, used to be split and grafted with BoneAlbumin and had been healing for 6 months. The newly formed bone had been histologically processed (dr. Glasz Tibor, 2nd Department of Pathology, Semmelweis University).

**Case 2 (Abb 3)**

For B.G. 65-year old male patient applied for prosthesis implantation with total tooth loss in lower jaw, and, in upper jaw with 4 frontal teeth residual roots.

While the operation we removed the roots of the teeth, we made sinus lift both sides of the quite thin upper jaw with 1—2mm width, and we grafted alveoles with BoneAlbumin. Panoramic radiography and CT images show the significant amount of bone grafting. On the CT-image, at most parts, bone height is around 12 mm.
Figure 3.3: Bone sampling from the place of tooth number 1.6., 6 months later.

Figure 3.4: Bone sample in the trepan, shows a living, bleeding bone, macroscopically.

Figure 3.5: Haematoxylin—eosin staining, 100x zooming. In tissue image, trabeculae are well-formed.

Figure 3.6: Haematoxylin—eosin staining, 200x zooming. Living bone tissue containing cells.

Figure 3.7: The 4 pieces of implants put into the upper right quadrant.

Figure 3.8: Panoramic radiography image following the implantation.

Figure 3.9: CT image on the alveolar crest in the period following the implantation.

Figure 3.10: Implant put in the place of tooth number 1.6., and the CT cross-section of the bone.
Following a 6-month healing and ossification period, at the place of the BoneAlbumin grafting, from the newly formed bone we made bone biopsy by bone trepan— as the first step of the preparation of implant bed. We sent the material to histological examination (dr. Glasz Tibor 2nd Department of Pathology, Semmelweis University).

While the implantation process—following the formation of implant bed by a magnetic hammer—there were 8 pieces of SGS implants put in.

**Case 3 (abb 4)**

B.J. 62-year old female patient had had fractured teeth for 4 years with 2 pieces of zirconia implants in the upper left molar region. We planned another zirconia implants instead of the broken ones, following the removal of the broken implants, bone grafting and another implantation process.

While the first operation we applied soft tissue expander, then with the help of bone trepan we removed the 2 pieces of broken implants. We split the knife edge ridge with the help of the engraver of the magnetic hammer, we made bone grafting, then we applied titanium mesh. While the second operation following the ossification process, to the augmented area we implanted 3 pieces of zirconia implants of Denti-type. On the implants, we put zirconia bridge.

**Figure 4.1:** B.J. panoramic radiography image of broken implants at the places of teeth number 2.6—2.7.

**Figure 4.2:** The image of the upper left molar region with the broken implants and minimal width of ridge.

**Figure 4.3:** Removal of the soft tissue expander.

**Figure 4.4:** Augmentation with BoneAlbumin, then application of titanium mesh, following the splitting of knife edged ridge.

**Figure 4.5:** Bone grafting, closed with titanium mesh.

**Figure 4.6:** Following a 9-month period of ossification, putting in zirconium implants, with implant bed formed with the help of magnetic hammer.
Case 4 (abb 5)

D.A. a 39-year old female patient with cysts on teeth number 3.6—3.7 in the lower left molar region came to us for treatment.

The cyst made the jaw so thin as the extraction of the teeth created the risk of break through the mandibular bone. While the first operation, we removed the dental crowns of teeth number 3.6—3.7 by air-turbine, then in the axis of dental neck plane, by burnishing teeth like seashells, we made longitudinal ducts with the help of fissure diamond bur. Into the ducts we placed cyst constricting equipment. 9 months after the cyst constricting process, with the help of engraver of the magnetic hammer, we removed the seashell-like remnants from the alveolus, in teeth number 3.6—3.7, then we made cystectomy. We grafted bone cavities with BoneAlbumin chips. 6 months after bone grafting, to the places of teeth number 3.6—3.7, where previously there were cysts, 2 pieces of SGS implants had been put in. We started the formation of the implant bed by bone trepan, thus we made histological bone-sampling according to the localization of the former cyst chamber. (dr. Glasz Tibor 2nd Department of Pathology, Semmelweis University). The samples of biopsy had been sent to histological examination.

Summarizing

Following the application of BoneAlbumin in oral surgery, dentistry and implantology, we can determine the following experiences:

• The advantages experienced in a 10-year application in orthopedic surgery are true for jaws as well, its application is advantageous, while it combines the several positive features of bone grafts.
Figure 5.4: Cyst constricting equipment and the seashell-like pieces of teeth remnants after their removal.

Figure 5.5: Cysts grafted with BoneAlbumin, following cystectomy.

Figure 5.6: Panoramic radiography image following cystectomy and BoneAlbumin grafting.

Figure 5.7: 6 months after the augmentation, bone sampling from the original place of the cyst, from BoneAlbumin.

From blood to bone.
In jaws, tissue integration is particularly good, according to clinical and histological finds, there is a living bone forming. Compared to other bone grafts, at the bone-graft border the demarcation is smaller. The new bone structure is very similar to the original own bone structure. The degree of resorption—in the present monitoring period—is significantly smaller the for the implanted own bone. There aren’t any granules and lifeless grains, such as there were in synthetic or xenograft bone graft materials.

In clinical practice, based on our experiences, positive features have continuously been proven, so BoneAlbumin may represent a significant breakthrough in bone grafting processes of oral surgery, dentistry and implantology.

In bone grafting in the fields of implantology and oral surgery, the application of BoneAlbumin opened up new avenues. Based on our experiences (in sinus-lifting, augmentation following bone-splitting, grafting process following extraction, augmentation, grafting bone losses, bone blocks, etc.), as for its behavior shows a transition between own implanted bone (autograft) and the bone of human origin (allograft). As a result of adding Albumin to it, in clinical practice, this material behaves as it was autograft, but with the application of it bone taking process—therefore, the second operation may be avoided. After mixing it with own blood or bone scrape, it results a bone even more similar to the living one than other bones of animal origin or synthetic ones, as well. Granules, blocks, spongiosa, corticalis human bones may be applied.

We consider the things said particularly important, knowing that with the continuous expansion of the average age the number of old people is growing, who lost their teeth but still live an active life. They have lost not only their teeth, but the significant amount of their bone stock, as well. In these cases, experts can reach success only with choosing the most humane bone shaping methods, tools and bone grafting materials.

Figure 5.8: Bone sample in the trepan shows a living, bleeding bone macroscopically.

Figure 5.9: At the place of the tissue sampling with trepan, there is living, hard, bleeding bone tissue.

Figure 5.10: Panoramic radiography image after the implantation made 6 months after the bone grafting.