Bone Grafts and Bone Graft Substitutes

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12.1 Introduction and Core Messages

Bone grafts or substitutes are used in spinal surgery to fill defects, to bridge defects or to promote spondylodesis. The physiological process is similar to that of fracture healing and incorporates the same spatial and temporal factors. The ideal material should provide osteogenetic, osteoinductive and osteoconductive properties. The traditional autologous bone grafts are probably still considered the "golden standard", but the problems associated with them bring up the need for substitutes. One alternative is the acquirance of allogenic or xenogenic bone grafts, which have specific problems of their own, which limit their use. The other aspect is the use of bone substitutes, which come in a growing variety of materials, shapes and application forms. Currently, none of these substitutes unite all of the prerequisites shown above, but they have the advantage of unlimited supply without causing additional problems such as donor site morbidity. And the combination of such substitutes as scaffold with the utilization of growth factors and mesenchymal stem cells brings with them a completely new array of possibilities.

12.2 Definition

12.2.1 Bone Graft

The bone is harvested from different parts of the patient. It is most commonly from the iliac crest but also from the vertebral structures, the ribs, the tibia as well as the fibula [1].

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12.2.2 Bone Graft Substitute

It replaces the autologous bone in order to achieve defect filling and bridging and also fusion [2]. It provides unlimited supply and eliminates donor site morbidity. But no substitute provides the combination of osteoinductive, osteoconductive and osteogenetic properties [1].

12.3 Physiology of Bone Regeneration

The bone is one of the few organs that retains the potential for regeneration throughout life. In contrast to other organs, the bone does not repair defects with scar material of poor quality but rather reinstates its original values. But fracture healing and therefore also bone regeneration are complex physiological processes.

Two basic principles of bone healing are described in literature [3] as follows:

- Primary bone healing ("direct healing") is very rare and not the usual form of healing achieved in spinal surgery.
- Secondary bone healing involves intramembranous and endochondral ossification and leads to callus formation. Callus formation is achieved through undifferentiated multipotent mesenchymal stem cells (MSCs) and requires cell vitality and blood supply.

In this cascade of bone regeneration, certain prerequisites are known. Most importantly, a vital cell population has to be present. MSCs have to be either present or transferred to the site via blood supply. These cells are transferred to a cell population with osteoblastic phenotypes.

In addition, the fracture haematoma offers a vast supply of signalling molecules (ILs, TNFs, TGFs, VEGF) to induce healing. Within the group of TGFs, the so-called bone morphogenetic proteins (BMP-2, BMP-7) have been extensively studied and shown to play a decisive role in the healing process [4]. The third important element is the extracellular matrix, providing a natural scaffold for the cellular interactions. This

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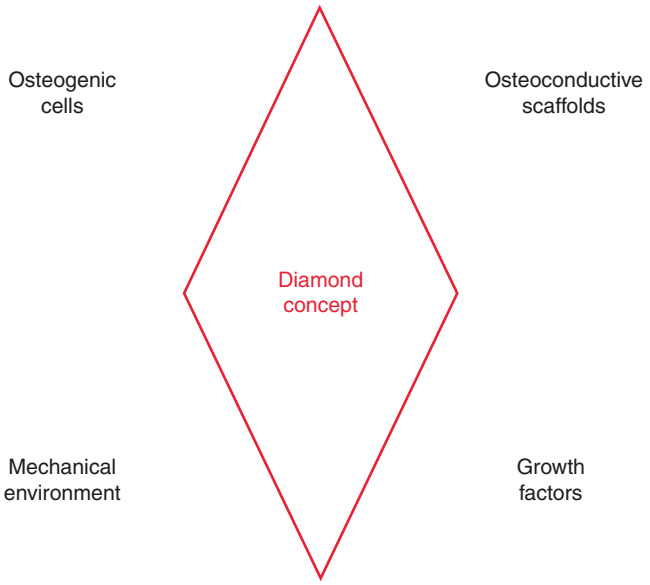

Fig. 12.1 "Diamond concept" regarding bone healing [5]

can be replaced by an immense number of osteoconductive materials such as allografts, demineralized bone matrix (DBM), hydroxyapatite and calcium-based ceramics, among others. These scaffolds have been shown to have an optimal pore size of 150–500 µm. The last important factor, important for fracture healing and bone formation, is the mechanical stability. All four components combined are described as the "diamond concept" (Fig. 12.1). It is well described in extremity fractures and of equal importance in spinal surgery [5].

12.4 Clinical Application

Therefore, bone or bone substitutes should preferably have the three properties mentioned above. **Osteogenicity** refers to the fact that they contain osteoblastic cells and are thereby capable of directly forming the bone. **Osteoconductivity** refers to the situation in which they provide a structure along which osteoblasts can attach and thereby the bone can grow. **Osteoinductivity** is the ability to induce nondifferentiated stem cells or osteoprogenitor cells to differentiate into osteoblasts. A "perfect" bone graft substitute would incorporate all three characteristics.

12.5 Autologous Bone Grafts

The "golden standard" of bone grafts is the autologous bone, although it is an area of growing controversy [1]. It is mostly harvested from the iliac crest, depending upon positioning of the patient. This donor site has the advantage of having a supply of the cancellous as well as cortical bone (tricortical graft) (Figs. 12.2 and 12.3).

Advantages

- Osteogenetic
- Osteoconductive
- Osteoinductive

Disadvantages

- Limited supply.
- High failure rate is reported.
- Risk of iliac crest fracture (Fig. 12.4).
- Correctional loss due to remodelling [6].
- Donor site morbidity (limited with correct utilization).
- Additional operation time.

Harvest sites

- Iliac crest (anterior, posterior)
- Locally (vertebral body, spinous process, lamina, etc.)
- Rib portion (in transthoracic approaches)
- Tibia/fibula

12.6 Surgical Technique of Iliac Crest Graft Harvesting

The bone from the iliac crest can be easily harvested. When choosing the anterior crest, one must be aware of the lateral femoral cutaneous nerve. On the other hand, a safety margin of at least 3 cm should be left from the anterior superior crest, where the hip flexion muscles derive from. We recommend harvesting the graft using a double-blade oscillating saw. The desired depth can also be harvested using a "graft cutter". This way a defined cortical graft is obtained, leaving room for additional harvesting of cancellous bone chips using a spoon. The defect is filled using a haemostatic pad, the fascia is closed and a drain should be placed to prevent a painful haematoma. Alternatively, according to the clinical application, "bone plugs" can also be harvested using special instruments (Fig. 12.5). This leaves less defect and can also be harvested in other locations.

12.7 Bone Graft Substitutes

These materials should ideally have the osteogenetic, osteoconductive and osteoinductive characteristics of an autograft without the substantial side effects. Most of these materials only provide osteoconductivity. Their integration into the bone substance can take place in different ways [7]. One way is the direct integration or resorption followed by conversion into the bone. The other way would be some kind of "graft-versus-host reaction" resulting in a self-contained graft or even a (partial) loss of graft substance without integration [8].

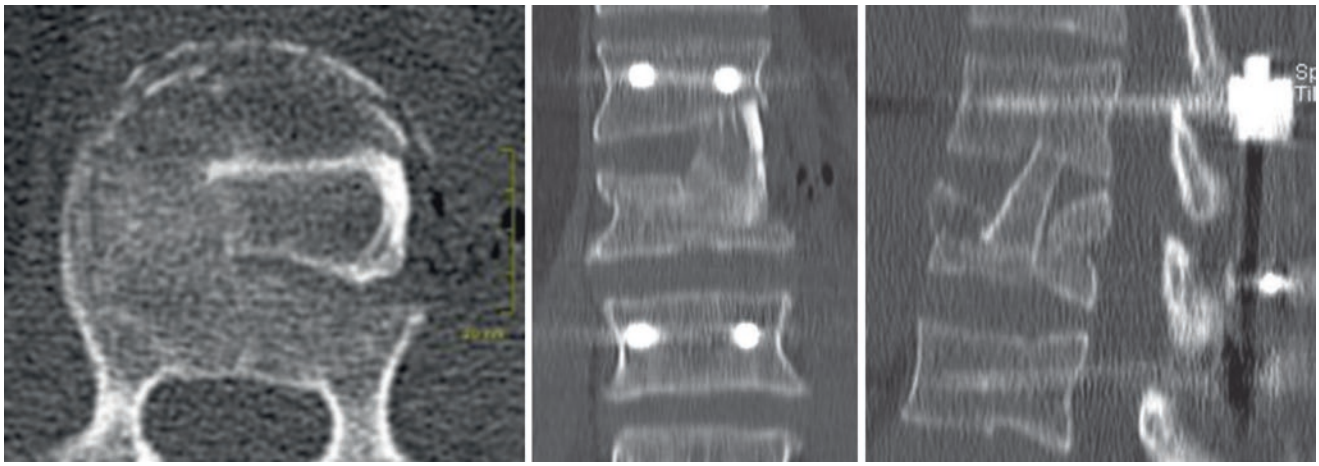

Fig. 12.2 CT scans in three planes documenting the correct size and positioning of a tricortical autograft

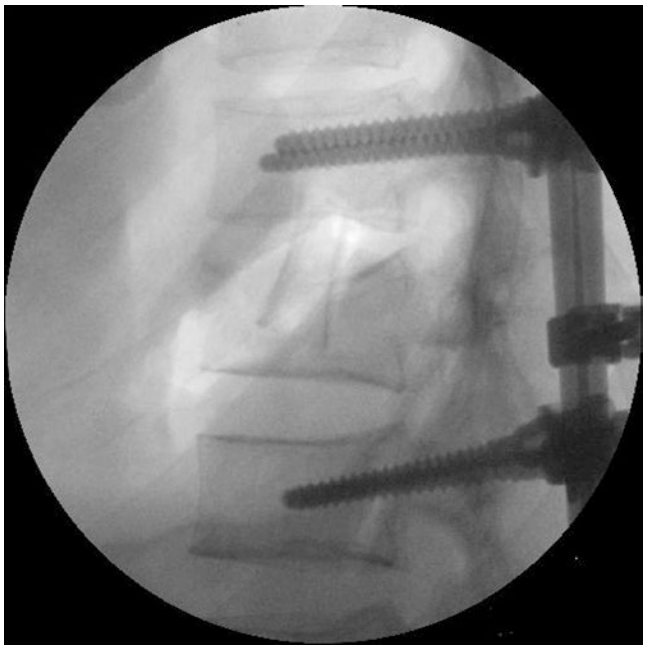

Fig. 12.3 Plain radiograph of a monosegmental, anterior spondylodesis with a tricortical iliac crest autograft following bisegmental, posterior stabilization

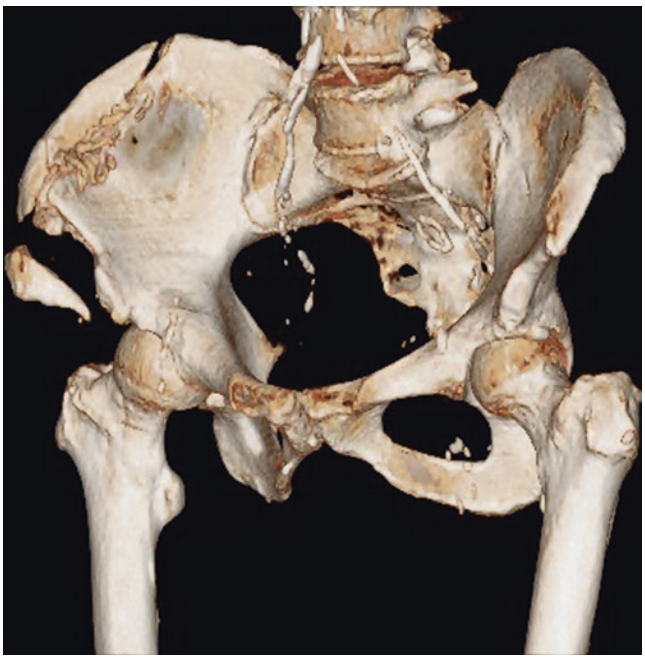

Fig. 12.4 Iliac crest fracture following bone harvest from the anterior iliac crest in the right side

12.8 Allografts

This relates to the tissue taken from one person for transplantation into another. This type of treatment has spread due to recent improvements in procurement, preparation and storage. Clinics with a high turnover of allografts have their own storage areas. This concept of bone banking is connected to a great deal of legal issues, showing great variations in different countries [9]. They are useful however to enlarge the volume of the autologous bone.

Advantages

- Osteoconductive
- Unlimited supply
- Multiple shapes and sizes
- No donor site morbidity

Disadvantages

- Not osteogenic (due to chemical processes in the making)
- Weak osteoinductive properties
- Possibility of infectious disease transmission

Fig. 12.5 Bone graft harvesting set (Synthes) used for different sizes of "plugs" (© by Synthes)

12.9 Demineralized Bone Matrix (DBM) and Bone Morphogenetic Protein (BMP)

DBM is a demineralized allograft bone with osteoinductive activity [10]. Demineralized bone matrixes are prepared by acid extraction of the allograft bone, resulting in loss of most of the mineralized components but retention of collagen and noncollagenous proteins, including growth factors. The efficacy of a demineralized bone matrix (DBM) as a bone graft substitute or extender may be related to the total amount of bone morphogenetic protein (BMP) present and the ratios of the different BMPs present. The multitude of different BMPs are all capable of recruiting bone-forming cells and encouraging local cells to aid in the bone formation process. There are up to now over 20 different BMPs known, but the clinical research is currently limited to BMP-2 and BMP-7. The different types of BMPs seem to show substantial variations in their osteogenetic potency. Recently, BMP has been associated with cancer, but further studies have found no correlation [11].

Advantages

- Osteoinductive with promoted bone formation [12].
- Osteoinductive potency is very variable in different products [4].
- Graft extender (in combination with autografts).

Disadvantages

- Poor structural integrity
- BMP alone not osteoconductive

12.10 Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) and Tricalcium Phosphate ($Ca_3(PO_4)_2$)

These substitutes are mainly known as bone void fillers. Taking into account their specific strengths (e.g. fast curing, fluid injection, etc.) and their weaknesses (low shear stress, poor biodegradability, etc.), new applications have arisen. These materials come in a wide array of different application forms (Fig. 12.6).

Advantages

- Osteoconductive (Fig. 12.7)
- Lasting stability
- Availability

Disadvantages

- Not osteoinductive
- Not osteogenic

Fig. 12.6 An array of different forms and shapes used in calcium phosphate bone substitutes (© by Synthes)

Table 12.1 Exemplary list of calcium phosphate products on the market (among others)

Product	Company	Type
Nanostim	Medtronic	Synthetic tricalcium
BoneSource	Howmedica	CaP cement
Alpha-BSM	DePuy	CaP cement
Calcibon	Biomet/Merck	CaP putty
MIMIX	Biomet	Synthetic tricalcium phosphate
Cerasorb	Curasan	Beta-tricalcium phosphate
ChronOS	Synthes	Beta-tricalcium phosphate
Vitoss	Orthovita	Beta-tricalcium phosphate
Pro osteon	Interpore cross	Coralline hydroxyapatite
Endobon	Biomet/Merck	Cancellous hydroxyapatite
BioFuse	Corin	Hydroxyapatite/CaP
Actifuse	ApaTech	Silicated calcium phosphate

12.11 Clinical Application

Current evolutions within this field, such as biphasic, injectable CaP and silicated CaP, widen the array of applications, offering a good supplement in achieving spinal fusion [13] (filling cages, lining cages, extending grafts, etc.) (Table 12.1). These substances should be rehydrated using the patients' blood before applying (Fig. 12.8).

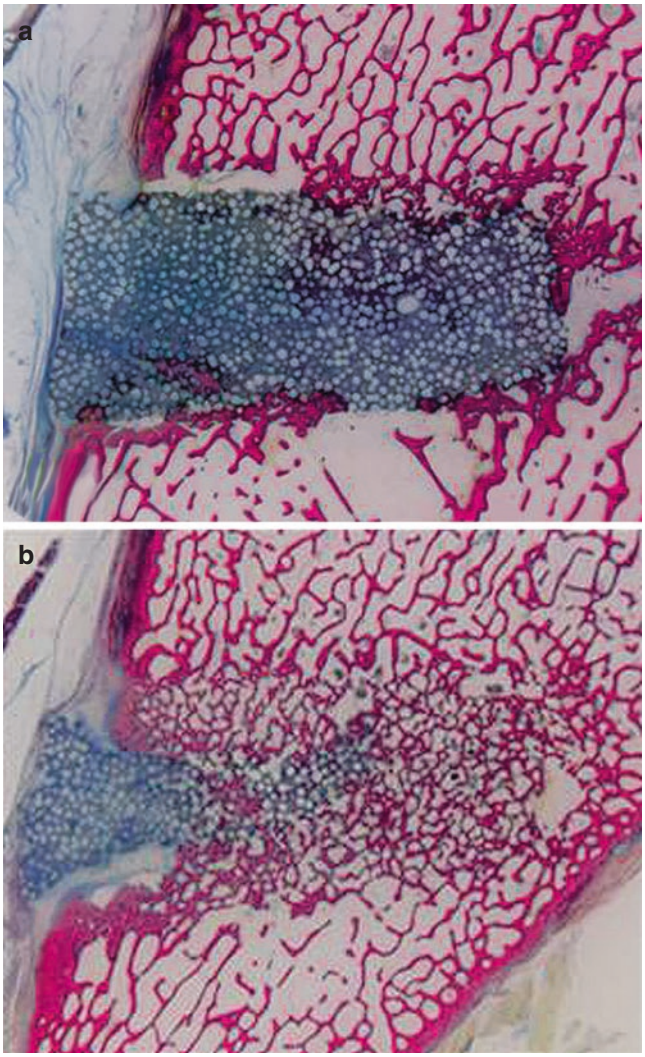

Fig. 12.7 (**a**, **b**) Histological findings using chronOS mixed with blood 6 weeks (**a**) and 12 weeks postoperatively (© by Synthes)

Fig. 12.8 ChronOS blocs mixed with blood (© by Synthes)

12.12 Other Ceramics (Sea Corals, Calcium Sulphate)

These substances are currently researched to evaluate their usefulness to supplement or even replace the ceramics in use today.

12.13 Outlook

Tissue engineering and the further development of growth factors offer great potential for the future of fusion and bone substitutes. Materials will evolve and offer "ideal" and individual solutions for specific indications [14]. But currently, the autologous bone is still the golden standard [15]. The diversity of current substitutes will make further comparative studies quite difficult.

References

1. Sen MK, Miclau T. Autologous iliac crest bone graft: should it still be the gold standard for treating nonunions? Injury. 2007;38(Suppl 1):S75–80.
2. Bone Graft Alternatives (according to the North American Spine Society). http://www.spine.org/Documents/bone_grafts_2006.pdf
3. Phillips AM. Overview of the fracture healing cascade. Injury. 2005;36(Suppl 3):S5–7.
4. Papakostidis C, Kontakis D, Bhandari M, et al. Efficacy of autologeous iliac crest bone graft and bone morphologic proteins for posterolateral fusion of lumbar spine – a metaanalysis of the results. Spine. 2008;33(19):E680–92.
5. Giannoudis PV, Einhorn TA, Marsh D. Fracture healing: the diamond concept. Injury. 2007;38(Suppl 4):S3–6.
6. Morrison RH, Thierolf A, Weckbach A. Volumetric changes of iliac crest autografts used to reconstruct the anterior column in thoracolumbar fractures: a follow-up using CT scans. Spine. 2007;32(26):3030–5.
7. Berven S, Tay BK, Kleinstueck FS, et al. Clinical applications of bone graft substitutes in spine surgery: consideration of mineralized and demineralized preparations and growth factor supplementation. Eur Spine J. 2001;10(Suppl 2):S169–77.
8. Schimandle JH, Boden SD. Bone substitutes for lumbar fusion: present and future. Oper Tech Orthop. 1997;7:60–7.
9. Friedlaender GE. Bone-banking. J Bone Joint Surg Am. 1982;64:307–11.
10. Petersen B, Whang PG, Iglesias R, et al. Osteoinductivity of commercially available demineralized bone matrix. Preparations in a spine fusion model. J Bone Joint Surg Am. 2004;86-A(10):2243–50.
11. Cooper GS, Kou TD. Risk of cancer following lumbar fusion surgery with recombinant human bone morphogenic protein-2 (rhBMP-2): an analysis using a commercially insured patient population. Int J Spine Surg. 2018;12(2):260–8.
12. Kwong FN, Harris MB. Recent developments in the biology of fracture repair. J Am Acad Orthop Surg. 2008;16(11):619–25.
13. Becker S, Maissen O, Ponomarev I, et al. Osteopromotion by a beta-tricalcium phosphate/bone marrow hybrid implant for use in spine surgery. Spine. 2006;31(1):11–7.
14. Giannoudis PV, Tzioupis CC, Tsirids E. Gene therapy in orthopaedics. Injury. 2006;37(Suppl 1):S30–40.
15. Morris MT, Tarpada SP, Cho W. Bone graft materials for posterolateral fusion made simple: a systematic review. Eur Spine J. 2018;27:1856–67.