**DIPLOMARBEIT**

# Allograft reconstruction in the treatment of musculoskeletal tumours a comparative analysis


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Graz, am……………….. (Unterschrift)

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# Abstract

Allograft reconstructions after wide resection have a long history and are quite popular in treatment of musculoskeletal tumours. Sarcoma patients are now having a considerable improved prognosis as a result of multimodal therapy concept, combining chemotherapy with wide resection and - when indicated - additional radiation, and a high percentage of generally young patients is now surviving their disease. In the light of these developments, durability of reconstruction is of growing interest.

It's the aim of this diploma thesis to work out how long allograft reconstructions last as well as the complications compromising the outcome and their frequencies.

Medical records of patients who received an allograft reconstruction at the Department of Orthopaedics Surgery Graz were scanned and two reconstruction types were analysed retrospectively. Six patients with osteoarticular allografts for reconstructions of distal radius and fourteen patients with a vascularised fibula combined with a massive allograft for intercalary reconstructions of lower limb formed these groups. Due to the low number of cases a literature review was done additionally to supplement and compare our results to answer the question of durability.

None of the allograft reconstructions performed at the Department of Orthopaedics Surgery Graz had to be removed. Five patients developed nonunion, three in the fibula group and two in the radius group. In the fibula group four patients sustained plate breakage with consecutive fracture and two patients developed infection. All complications were treated successfully without compromising the final outcome. In literature similar results in terms of complication rates and encouraging survival rates were found for these reconstruction types. In literature review it could be further worked out that intercalary allograft and allograft prosthetic composite reconstructions are durable and likely to last for the whole duration of patients' life. In osteoarticular allografts around the knee, however, complication and failure rates were found to be quite high and survival rates were discouraging.

Osteoarticular allografts are probably one of the best solutions for reconstructions of the distal radius, but at other anatomic regions they aren't providing a durable

reconstruction, because of their high complication and failure rates. Intercalary allografts, especially in combination with an autologous vascularised fibula and allograft prosthesis composites, however, provide a durable reconstructive solution. Allografts are a great option in limb salvage surgery, but their usage must be considered together with other reconstructive alternatives in regard of the localisation and characteristics of tumour as well as of patient's needs and expectations.

# Kurzfassung

In der Behandlung von Knochen- und Weichteiltumoren haben Allografts eine lange Tradition und sind eine beliebte Möglichkeit um die, durch weite Resektion entstandenen, knöchernen Defekte zu rekonstruieren. Durch ein multimodales Behandlungskonzept unter Kombination einer Polychemotherapie mit einer chirurgisch weiten Resektion und gegebenenfalls ergänzender Bestrahlung konnte die Prognose der meist jungen PatientInnen mit Knochen- und Weichteiltumoren deutlich verbessert werden. Anbetrachts dieser Entwicklung, ist die Beständigkeit einer Rekonstruktion mit einem Allograft von wachsendem Interesse.

Ziel dieser Diplomarbeit ist es auszuarbeiten, wie lange diese Knochenrekonstruktionen allen Alltagsanforderungen stand halten, sowie die Art und Häufigkeit der auftretenden Komplikationen zu ermitteln.

Die Krankenakten aller Patienten, die eine Knochenrekonstruktion mit einem Allograft an der Universitätsklinik für Orthopädie und orthopädische Chirurgie Graz erhalten haben, wurden aufgearbeitet und zwei Gruppen von Allograft Rekonstruktionen wurden retrospektiv analysiert. Sechs Patienten mit artikulierenden Allografts zur Rekonstruktion des distalen Radius sowie vierzehn Patienten mit Allografts in Kombination mit einer autologen gefäßgestielten Fibula zur Rekonstruktion interkalärer Defekte an der unteren Extremität bildeten diese Gruppen. Da die Gesamtzahl der Patienten mit solchen Knochenrekonstruktionen gering ist, wurde zusätzlich eine Literaturrecherche durchgeführt, um die Ergebnisse mit anderen zu vergleichen und um die Frage nach der allgemeinen Beständigkeit von Allografts nach Möglichkeit zu beantworten.

Keine der an der Universitätsklinik für Orthopädie und orthopädische Chirurgie Graz durchgeführten Rekonstruktionen mit einem Allograft musste aufgrund von Komplikationen entfernt werden. Fünf Patienten entwickelten eine Pseudarthrose, drei mit Rekonstruktionen an der unteren Extremität und zwei mit Rekonstruktionen des distalen Radius. Weiters kam es bei vier Patienten mit Rekonstruktionen mit einer gefäßgestielten Fibula und einem Allograft zum Bruch der Platte mit konsekutiver Fraktur des rekonstruierten Knochens und in zwei Patienten dieser Gruppe infizierte sich die Knochenrekonstruktion. Alle Komplikationen konnten erfolgreich behandelt werden. In der Literatur konnten in

Bezug auf Komplikationsraten ähnliche Ergebnisse für diese beiden Verwendungen von Allografts gefunden werden, sowie vielversprechende Überlebensraten. Die Literaturrecherche ergab weiters, dass Rekonstruktionen mit interkaläre Allografts und Composite Allografts den Alltagsbelastungen standhalten und die gesamte Lebensdauer des Patienten überstehen können. Über artikulierende Allografts, vor allem um das Kniegelenk, wurden hohen Komplikationsraten und häufige Misserfolge berichtet.

Artikulierende Allografts zählen nach Resektion des distalen Radius zu den besten Rekonstruktionsmöglichkeiten, aber zur Rekonstruktion knöcherner Defekte an anderen Lokalisationen bieten artikulierende Allografts aufgrund der hohen Komplikationsraten und häufigen Misserfolge keine beständige Lösung. Interkaläre Allografts, vor allem in Kombination mit einer autologen gefäßgestielten Fibula, und Composite Allografts sind allerdings eine dauerhafte Rekonstruktionsmöglichkeit. Allografts sind eine hervorragende Möglichkeit zur Rekonstruktion knöcherner Defekte nach weiter Resektion, aber ihr Einsatz sollte gemeinsam mit anderen Möglichkeiten in Hinblick auf Tumoreigenschaften, Lokalisation sowie auf die Bedürfnisse und Erwartungen der einzelnen PatientInnen bedacht werden.

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# Abbreviations

| | |
|---|---|
| a.p. | anterior - posterior |
| APC | Allograft prosthesis composite |
| BMP | Bone Morphogenic Protein |
| CITO | Central Institute of Traumatology and Orthopaedics, Moscow |
| CTX | Chemotherapy |
| DASH score | Disabilities of the Arm, Shoulder and Hand score |
| DMB | Demineralised bone matrix |
| DOD | Dead of disease |
| DRUJ | Distal radioulnar joint |
| e.g | for example (Latin exempli gratia) |
| ESWT | Extracorporeal shock wave therapy |
| et al. | and others (Latin et alii) |
| GCT | Giant cell tumour |
| HCV | Hepatitis C Virus |
| HHS | Harris Hip Score |
| HIV | Human Immunodeficiency Virus |
| HLA | Human Leukocyte Antigens |
| MGH | Massachusetts General Hospital |
| MUG | Medical University of Graz |
| MSTS | Musculoskeletal Tumor Society Score |
| n.s | not specified |
| PCR | Polymerase Chain Reaction |
| RNA | Ribonucleic acid |
| RTX | Radiation |

# 1 General part

## 1.1 History

Bone allografts as biological substitute have been used to reconstruct skeletal defects for a long time. If Genesis 2 is neglected, Macewen (1) first reported in 1887 about allografts to replace bone. He referred to five cases of successful reconstruction of skeletal defects with the use of bone grafts. In one case he fragmented cortical bone - witch he obtained from patients undergoing an osteotomy to rectify marked anterior tibial curves - and used the bone grafts to rebuild a humerus. Thirty years later the patient had a normal functionally limb and could work as a joiner (2). Lexer demonstrated in 1908 the use of allografts from fresh amputated limbs for various techniques of fixations and reconstructions of facial and limb defects. He also was first to transplant whole or hemijoint allografts and in 1925 he reported that 50% of these patients were doing well 15 years after the operation.(3-5) This concept however did not find general acceptance. Herndon and Chase (6, 7) as well as Curtiss (8, 9) discovered during their investigations that freezing reduced the immune response. These results led to study series of bone allografts in humans using frozen bone grafts. Ottolenghi (10), Volkov (11) and Parrish (12) published good results as they used massive frozen allografts to reconstruct skeletal defects after tumour resection, but declared that the outcome was unpredictable.

Allograft transplantation was facilitated by the establishment of bone banks, like the CITO bone bank in Moscow 1956 (13), or the MGH Bone Bank in 1974 (14).

In the 1980s with the improvement of chemotherapy, the survival rate for patients with sarcomas increased markedly and they begun to outlive their disease. (15-23) Since it could have been demonstrated that limb salvage does not compromise this improved survival and has as well advantages, like better function, better emotional acceptance and cost effectiveness compared with amputation (24-26), massive allografts have been used widely to reconstruct large bone defects after tumour resection. (13, 14, 27-33)

## 1.2 Types of bone grafts

Bone grafting is a common used technique in orthopaedic surgery in general. Varying types of bone grafts are available differing in their biological and mechanical properties. Qualities and potential assets and drawbacks of all sorts of bone grafts must be considered to choose the right graft for each indication. (4, 34-36)

### 1.2.1 Autografts

Autogenous bone graft is the transplantation of bone taken from one anatomic site to another site in the same individual. (35) Complete histocompatibility and no opportunity of disease transmission are advantages of all autografts. Whereas limited availability, the increased surgical time and the possibility of donor side morbidity, like infection, prolonged drainage, chronic pain, gait disturbance – common if iliac crest is harvested – nerve injury or muscle weakness are noteworthy drawbacks of autogenic grafts.(4, 34, 35, 37-42)

#### *1.2.1.1 Autologous cancellous bone grafts*

Autologous cancellous bone can be procured quite easily from several anatomic sites as from iliac crest – most common site with more cancellous bone available than from other sites – distal radius, proximal tibia, distal femur or greater trochanter. (4, 43)

The nature of autologous cancellous bone grafts, which consist of an intimate trabecular structure lined with osteoblasts and a large surface area, is responsible for their osteogenic, osteoinductive and osteoconductive properties, making them attractive at sites where new bone formation is desired. (34, 35) Therefore bone grafting with cancellous autografts is gold standard for management of bone defects and nonunion. (4, 34, 43)

Osteogenesis is the synthesis of new bone and is induced by osteogenic precursor cells and osteoblasts within a graft. To have osteogenic properties a graft has to contain living osteogenic precursor cells and osteoblasts, whereas osteonecrosis during preparation would compromise these properties. Careful harvesting techniques and adequate interim storage has to be kept in mind to avoid osteonecrosis and to conserve viable cells. (34-37, 44)

Osteoinduction is recruitment of mesenchymal stem cells at and around the host side to differentiate into osteoblasts. The osteoinductive properties of a graft depend on the availability of growth factors, as bone morphogenic proteins (BMP-2, BMP-4 and BMP-7) and angiogenic factors (vascular endothelial growth factor and fibroblast growth factor), and on the presence of inducible cells in the graft bed. (34-36, 44)

Osteoconduction is the process by which ordered and three-dimensional ingrowth of capillaries, perivascular tissues and mesenchymal stem cells happens from the host site along the implanted graft to allow even distribution of new bone in the grafted volume and to enable union with the local host bone. The graft acts as a scaffold for ingrowth of vessels and cells from the host bed. Osteoconductive properties and with them incorporation of a graft depends on its three-dimensional structure and its surface. Cancellous grafts which are highly porous and have a large surface are incorporated much faster than dense cortical grafts. (35, 36, 44)

Featuring these three properties autologous cancellous bone has the best potential to provide new bone formation and graft incorporation but it does not provide any mechanical stability. If stability of the bone graft is required – additional to its bone forming properties – a cortical graft must be used. (34)

#### *1.2.1.2 Autologous cortical bone grafts*

Cortical autografts have varying mechanical and biological properties depending on the way how they are used. Unprocessed cortical autografts have similar properties as cancellous autografts and provide mechanical strength. It is as well osteogenic, osteoinductive and osteoconductive, but the number of viable cells contained in the graft is lower reducing its osteogenic quality and the dense architecture compromises its osteoconductive properties. The process of graft incorporation is described as creeping substitution which stands for resorption and replacement of the graft's scaffolding with new host bone. Although revascularisation and graft incorporation go on more slowly the end result is full graft incorporation by complete resorption of the graft with concomitant replacement with new viable bone. (34, 35, 43, 44)

Vascularised cortical autografts accelerate these processes. This is caused by the main advantage of vascularised cortical autografts, its independent vascularity which ensures immediate proper blood supply. Due to its vascularity the graft remains viable and as living tissue it unites more rapidly, has a high remodelling capacity similar to normal bone and is more resistant to infection than nonviable grafts. (4, 34, 35, 43, 45-50) Reconstruction with vascularised bone grafts is a lengthy and technically demanding surgical procedure requiring orthopaedic and microvascular skill sets. Limited supply and mostly inappropriate dimensions are also disadvantages of this procedure. (4, 34, 38, 39, 45, 47, 50, 51) The fibula and iliac crest are the most popular vascularised autografts. (45, 47)

Utilising the particular shape of the bone, vascularised iliac crest is mainly used in mandibular and maxillary defects. Especially in mandibular reconstructions iliac crest is superior to other grafts in terms of height and proper curve. While iliac crest's shape makes it attractive for mandibular reconstructions, this makes it simultaneously inappropriate for reconstructions of long tubular bones, although its sporadic usage for shorter defects in tubular bones has been reported. (40, 42, 47, 52-54)

Vascularised fibula graft is frequently used for large segmental defects in long tubular bones. As a long cortical bone fibula provides a stable strut to bridge huge bone gaps (50) up to 30 centimetres (47) and although the fibula is narrow and weaker than the resected bone, it responds with hypertrophy to biomechanical loading. (4, 49) But until hypertrophy has ceased there is an increased fracture risk in fibular reconstructions requiring prolonged immobilisation and protected weight bearing. (4, 39, 47, 49, 51, 55) The low initial mechanical strength results in the very fact that the fibula as a sole bone replacement is mainly done in non weight bearing reconstructions like the humerus. (46, 56) To improve mechanical strength and reduce fracture risk the vascularised fibula flap can be used as double-barrelled fibula. This provides a strong and stable construct by transferring twice the volume of a fibula bone to a given length without additional vascular anastomosis. (46, 56) A vascularised fibula is also frequently used in combination with a massive bone allograft, particularly in weight bearing reconstructions of the femur or the tibia. This combination unites the excellent biological properties of the viable vascularised fibula and the mechanical strength of the allograft. It offers shorter period of immobilisation and protected weight bearing, faster union, better graft incorporation and lower infection rates compared to reconstruction where fibula or allograft are used alone. (4, 46, 48)

Vascularised bone grafts are not only used to fill defects or to augment other reconstructions, they are also applied successfully in treatment of nonunions following fracture as well as in allograft constructs. (45, 57, 58)

For orthopaedic surgeons dealing with bone tumours, tumour freed orthotopic autografts are an option, especially in cultures where allograft procedures is declined for social and religious reasons. (47) There are several ways to get the bone tumour free, but the general procedure is always similar: First en bloc resection is done then tumour destroying is done, either by extracorporeal irradiation or by pasteurization. The soft tissue bulk is removed before or after extracorporeal tumour treatment depending on the method and the bone is replaced and fixed intramedullary or with plate and screws. Advantages of these types of autografts are the avoidance of disease transmission and immunologic response, the perfect size match and the ease of procurement. These methods are contraindicated if there is a significant loss of structural integrity caused by osteolytic tumours. (46, 47, 59-62)

Pasteurization is a treatment of heat at 60 – 65°C for 30 – 40 minutes, which has a lethal effect on malignant cells while preserving osteoinductive property, since biological activity of BMP – responsible for osteoinduction – is only destroyed in thermal exposures greater than 70°C. Pasteurization seems to preserve sufficient biomechanical strength and good osseous integration. (59, 63) No local recurrence occurred in Manabe’s series of 23 pasteurised autologous bone grafts, demonstrating that it is also a safe method. (59) Infection, fracture and nonunion rates were similar to those reported in allograft reconstructions illustrating that pasteurised autografts are a suitable alternative to autografts.

For extracorporeal irradiated autografts the optimal dose of irradiation will need to be determined. (46) High doses affect the biological and biomechanical properties of a bone graft leading to a high risk of fracture and non-union. At doses between 1 and 5 kGy irradiation incorporation is delayed in autografts – compared with untreated autografts – but autologous bone grafts retain most of their biological properties. (64) The intention must be to choose a dose by which complete tumour control is achieved without compromising graft performance too much. Poffyn et al. (60) used an irradiation dose of 300 Gy and observed only one local recurrence in surrounding soft tissue in 108 extracorporeal irradiated autografts, indicating that this dose is safe. Chen et al. (62) compared extracorporeal irradiated autografts with allografts and found only slightly higher fracture rates in irradiated grafts and lower nonunion rates in autografts than in allografts. All fractures in irradiated autografts healed after immobilisation in a cast suggesting that irradiation doesn't affect biologic properties of the bone adversely. This goes well with the observations of Poffyn et al. (60) who found active bone remodelling with viable osteocytes in lacunae as well as bone apposition and regeneration at the surface and within the bone.

Both Poffyn (60, 61) and Chen (62) achieved good results with complication rates similar to allograft reconstructions, supporting extracorporeal irradiated autografts as an acceptable alternative to allograft reconstructions.

### 1.2.2 Allografts

An allograft is a bone transferred between two genetically dissimilar individuals of the same species. (35) Allografts are an attractive option in reconstruction of skeletal defects and the main issue of this thesis. It is the most used bone substitute in Europe. Their supply is less limited than the supply of autografts and donor side morbidity is obviated. Especially for corticocancellous bone allografts and bone morsel, the femoral head of a patient undergoing a hip replacement is a convenient source of bone. Bone procurement from multi-organ donors under sterile conditions in the operating theatre is the most likely mean to obtain massive bone allografts for orthopaedic oncology. Safety of allografts is a major concern requiring extensive donor screening. (35, 36) The risk of disease transmission together with other disadvantages and advantages of allografts will be discussed in an extra chapter with a focus on massive bone allografts. (see 1.4 Assets and drawbacks of massive bone allografts)

#### *1.2.2.1 Cancellous allografts*

Cancellous allografts are poor promoters of bone healing compared with their autologous counterparts. (35) To reduce immunologic response allografts are frozen and they contain no viable cells so that allografts are not osteogenic. (43) Revascularisation and remodelling is inferior and slower but resorption as well as osteoconduction and osteoinduction is proceeding. The cancellous bone grafts act as a scaffold onto which new bone is laid down by the host. Cancellous allografts are incorporated faster and more completely than cortical allografts, since revascularisation is easier in them so that resorption and bone formation can occur concomitantly. (35, 43, 44)

Cancellous allograft chips are commonly used to fill small segmental defects. (35)

### *1.2.2.2 Demineralised bone matrix*

Mild acid extraction of bone removes the mineral phase of bone while leaving behind bone proteins (BMPs), growth factors, collagen and noncollagenous proteins. (35) Demineralised bone matrix (DMB) has an osteoinductive property since it contains two factors necessary for osteoinduction namely human BMP and collagen type I. Since DMB is acellular, its success depends on the vascularisation and the cellular environment of the host bed. DMB can be mixed with cancellous allograft chips, calcium sulphate, calcium phosphate or tricalcium phosphate to increase its osteoconductive potential. Various ready-for-use formulations with DMB combined with different carrier substances and additives are available and mainly used in treatment of nonunions. (35, 36, 43)

### *1.2.2.3 Massive cortical allografts*

Cortical allografts are one popular option in limb salvage surgery. Massive bone allografts serve as a spacer allowing osteoconduction of host cells into its mass followed by progressive incorporation and provide mechanical strength able to resist and transmit loads. (36) Graft incorporation happens by creeping substitution meaning resorption and replacement with new bone. In cortical bone grafts bone formation occurs only after resorption. The resorptive pattern dominates the first two years weakening the graft, which is reflected in the increased incidence of fractures during this time. Theoretically the entire graft is replaced by host bone, but effectively this process is incomplete and a final bulk of necrotic bone remains hardly substituted by new bone. (36, 44, 65, 66) Enneking et al. (66) found in their observations on retrieved allografts that internal repair is taking place very slowly, confined to the superficial surface and the ends of the graft and involves only 20% of the graft by 5 years. The deep unrepaired portions of the graft retained their architecture. The main factors of bone incorporation – revascularisation, new bone formation and host-graft union – are affected adversely by processes reducing the biological activity of the graft like freezing, histocompatibility antigen disparities between donor and recipient, mechanical instability and local or systemic treatment compromising the biologic activity of the graft and surrounding tissue like irradiation or chemotherapy. (67) Perforation of cortical bone allografts have been done to improve their incorporation. Indeed it improved the amount of newly formed bone but it's not advisable since cortical perforation increases fracture risk. (68-71)

Massive bone allografts are used in several ways as intercalary allografts using a bone segment similar to the one removed, as segmental allografts in arthrodesis mainly in the knee and the ankle or as segmental allograft in combination with prosthesis, known as allograft prosthesis composite. Massive bone allografts can also be used as osteoarticular allografts, for partial joint reconstruction, (36) as all allografts osteoarticular allografts are frozen to reduce their immunogenicity. Before freezing, the articular cartilage is treated with glycerol or dimethyl sulfoxide for cryopreservation. (35) But in spite of cryopreservation, the viability of articular cartilage poorly preserved. Ginat et al. (72) retrieved and studied an osteoarticular allograft of the proximal humerus 18 years after implantation. Although they found viable bone marrow and bone, the remaining hyaline cartilage was completely nonviable. Enneking et al. (65) found in their observations on 73 retrieved allografts also no survival of chondrocytes in the articular cartilage. Late degenerative changes in the articular cartilage coincided with subchondral revascularisation and fragmentation and the articulating surface got covered by a pannus of fibrovascular reparative tissue. (65) Joint degeneration occurs in nearly all osteoarticular reconstructions within the first five years. Radiographic signs normally are worse than clinical symptoms, since the allograft is a dead bone with no neurological feedback resulting in a long lasting pain-free course unless the joint has significant signs of incongruence. (14, 73-80) Mankin et al. (81) found osteoarthritis becoming a problem at approximately 6 years. 16% of the patients with osteoarticular allografts required total joint replacement. Joint survival rates at ten years in weight bearing joints without the need of total joint replacement are reported between 65% and 80% (82-84)

## 1.3 Immunogenicity of bone allografts

The success of bone allografts may be related to the relative low antigenic nature of processed bone. (45) Now there is ample evidence that allogenic bone is immunogenic especially with respect to cell surface histocompatibility antigens. Fresh allogenic bone grafts evokes most intense immune response while freezing and even more after freeze-drying of bone has been proven to reduce this response. (9, 14, 45, 85-89) In the canine model of Friedlaender et al. (87) fresh allografts and – to a lesser degree – deep frozen corticocancellous bone evoked detectable humoral and cell-mediated immunity whereas freeze-dried cortical bone allografts failed to sensitise the recipients. Strong et al. (86) were able to demonstrate sensitisation to Human Leukocyte Antigens (HLA) after frozen allograft transplantation. Among the recipients the overall sensitisation was 67%.

Since processed (removing of bone marrow) frozen bone allografts are not containing any viable antigen presenting cells, they must trigger an indirect pathway of allogenic recognition in recipient. (90) The nonviable allograft releases slowly – but during a long period – antigens from dead cells. Collagen and matrix can evoke an immune response but the major source of bone-graft immunogenicity are cell-surface transplantation antigens controlled by major histocompatibility complex. (88) Taken up by host antigen presenting cells T-cells recognise these antigens. So by an indirect pathway allogenic bone can activate T-cells of the killer/suppressor phenotype and induce their proliferation. This kind of response is specific to major histocompatibility of both class I and class II. (85, 88) The graft antigens can either release a chronic type of rejection or they can create an immunologic state of tolerance to grafted antigens. The latter may explain the difficulties in correlating HLA mismatch with frozen bone allografts. Another explanation for these difficulties is that maybe some mismatches are more immunoreactive than others. (90) Not all immune responses are the same and not all immune responses are necessarily harmful. (88)

The immunologic interaction between host and graft has an effect on graft incorporation. (89) There is a relationship between cells and cytokines of immune system and those of the bone remodelling system, since cytokines generated by immunocompetent cells (e.g. transforming growth factor-β, interleukin-2, interleukin-6) play also an important role in bone remodelling. (85, 88, 91) Histocompatibility antigen disparities between donor and recipient affects bone graft incorporation adversely. Revascularisation is delayed or inhibited and new bone formation is compromised in mismatched frozen bone grafts. (67) The host-versus-graft reaction may occur to a variable degree from rapid dissolution of the graft to walling of with almost no vascular invasion. (14,78,79) As immunogenicity of allografts influences graft incorporation, it suggests itself that complications related to delayed revascularisation and compromised new bone formation as infection, fracture and nonunion are also immunogenic directed and signs of subtle rejection. (14, 28, 92)

Friedlaender et al. (85) observed no differences in complication rates but patients without sensitisation to class II antigens achieved better results than sensitised ones. The improved long term results in patients matched for HLA class II may reflect more successful biologic incorporation. Muscolo et al. (90) found patients matched for one or two HLA class I antigens scoring higher than totally mismatched while HLA class II and AB0 seemed not to have an influence on radiographic outcome. These findings suggest that immune response evoked by frozen bone allografts might be related with low radiographic outcomes and that matching with regard to major histocompatibility complex may improve these results. (85, 90)

Since matching in major histocompatibility complex Class II antigens showed an effect on graft survival and that preoperative or postoperative transplant sensitization of Class II antigens influences the outcome in a negative way it seems likely that results could be improved by either immunosupression or better matching of host and graft. Immunosuppressive drugs have severe sight effects and a mortality rate on their own so that “life-threatening drugs would be applied for a limb-threatening disease” in a patient already weakened by malignant disease and its treatment. Immunosuppressive drugs are not recommendable for oncologic patients (73) as suppressing the immune system in patients with high grade sarcomas may increase the distribution rate and the growth rate of micrometastases. (14, 80, 92) The problem with better matching between donor and host is a practical one, because it is difficult to match them in size and shape as well as for major histocompatibility complex and this would need improved networking of large bone bank. To draw clear conclusions about the improvement of allograft results by matching further researches have to been done. (14, 92)

## 1.4 Assets and drawbacks of massive bone allografts

Massive bone allografts are frequently used as a natural substitute to repair skeletal defects primarily in limb salvage procedures in orthopaedic oncology. They permit an anatomical reconstruction with the ability to union biologically to host bone through callus formation. (36, 47) The bone graft is incorporated gradually by creeping substitution, what offers longevity of reconstruction. (41, 45, 93) Allografts enable the reconstruction of long bony defects restoring bone stock and allow better soft tissue attachment, as tendon reinsertion, than in endoprosthetic reconstructions. (36, 41, 46, 62) Theoretically these features result in better limb function, compared with endoprostheses. (78) If an allograft is used for reconstruction the duration of surgical procedure is considerable shortened compared to the usage of autografts. (29) Allografts are not that limited in availability as autografts are. They are relatively easy obtained and can be sized and stored for a long period. (34, 36, 41) Donor side morbidity is no issue in allografts. (29, 35, 36)

Although the use of massive allografts is generally accepted especially in Asian countries it is avoided for cultural or religious reasons. (47)

Allografts bear the risk of disease transmission. Bacterial contamination can be life-threatening if it occurs. (36) To avoid this allografts are harvested under sterile conditions and each bone is cultured at least once. Buck et al. (94) even suggested that larger bones should be cultured three times to get samples from the superficial, the marrow and the joint and during bone processing additional microbiologic cultures are taken. If any contamination is found the allograft is discarded. Allograft infection due to contamination is rare. In most cases of allograft infection no evidence of graft contamination could be found. (94-97) Viruses are even more difficult to track. There are well documented cases about transmission of the hepatitis C virus (HCV) as well as of the human immunodeficiency virus (HIV) through bone grafts. (36, 98-103) The cases of HIV transmission happened in the 1980s when no or no sensitive tests were available. Today more sensitive serologic tests for HIV antibodies, HIV antigens and polymerase chain reaction (PCR) are available and the donor's history is screened for any risk factors. It has also been shown that removal of blood and bone marrow by processing reduces the risk of viral disease transmission. (14, 63, 94, 97, 104, 105) Reviewing the reports of HIV transmission makes clear that all reported cases of virus transmission could have been prevented by using today's screening methods and the stringent donor selection standards. (5, 97, 98) The estimated risk to obtain an allograft from an unrecognized HIV infected donor is one in 1, 6 millions. (94) The last reported cases of HCV transmission by bone grafts happened in 2002. An antibody-negative donor infected eight bone and tissue recipients with HCV. After the virus disease occurred in the recipients, the frozen stored donor blood samples were examined again and HCV RNA was found. HCV nucleic acid testing wasn't done routinely to screen the donors in this institute, but would have prevented the disease transmission (100). Improved screening methods, multi-step screening and stringent donor selection guidelines made allografts safe and the risk of disease transmission is remote, although there is still the possibility of transmission of unknown pathogens.(5, 36, 97, 106)

To achieve good results and to avoid complications, best possible matching of the allograft in shape and size should be aimed among other things. A bone bank is necessary to ensure the availability of fitting and safe allografts. (14, 30, 77, 94, 107)

Compared with endoprostheses the surgical technique to implant an allograft is more demanding and the operation time is elongated. The rehabilitation time is also prolonged, which is a considerable drawback especially in patients with restricted life expectancy. (78, 91, 108-110)

The major disadvantage of allograft reconstruction is the relatively high complication rate. The most common complications associated with allografts, infection, fracture, nonunion and instability of joint (14, 45) will be discussed in detail. Endoprostheses, however, share some of these complications and implicate also additional problems as prosthetic loosening and wear. (78,111-114)

### 1.4.1 Infection:

One of the main complications in allograft procedures is infection with occurrence reported from 0 up to 30% (13, 14, 29, 30, 33, 45, 73, 74, 78, 80, 81, 83, 84, 92, 93, 95, 96, 115-121). Infection is the most devastating complication. It bears a high risk of loss of limb because infection is not easy to prevail. (36, 78, 80, 122, 123) Almost all infected allografts fail, since infected grafts have to be removed. In most cases a two stage procedure is proposed, an antibiotic loaded cement spacer is inserted and systemic antibiotics are administered. After a few months, when the infection is cleared, another allograft or a metallic device can be inserted. With this procedure limb salvage is possible in a reasonable number, but in some cases amputation is still the only possibility to contain infection. (83, 95, 108, 122) Mankin et al. reported a 10% infection rate, but also found infection causing 39% of all failures. (14) The same author showed in another paper that the amputation rate was higher in patients with infected allografts (25%) than in the entire group (3%), demonstrating that infection is a limb-threatening complication. (92) No matter if the limb can be saved or has to be amputated, existence of infection decreases the final outcome statistically. (92, 95)

Bacterial contamination of the allograft can be a reason for infection, although everything is done to obviate this, Liu et al. (96) reported that 4.6% of culture positive allografts were implanted and 75% of this contaminated allografts became infected. Also 1.6% of the culture negative allografts became infected. These results suggest that bacterial contamination must be avoided, because there is a high infection risk if it occurs. But they also show that bacterial contamination isn't the only reason for allograft infection since 25% of the culture positive allografts didn't get infected and also non contaminated grafts developed infection.

The allograft is prone to infections which could normally be eliminated by the host defenses or antibiotics or both. A large part of the allograft remains unchanged for several years and this large piece of dead organic tissue may serve as a nidus for infection. (5, 95)

Tomford et al. found no infections in small allografts like femoral head grafts and small bone and soft tissue allografts, but a 5% infection rate in large allografts in reconstruction after tumour resection, even 10% after malignant tumours and 4% infections in revision hip arthroplasty. (118) In series where the distal part of the radius was replaced with an allograft to treat giant cell tumour (GCT) no infections occurred. (116,124-127) In endoprosthetic reconstructions after tumour resection infection rates are reported from 0 to 34% nearly the same as in biological reconstructions. (108-110,128-138) On account of these results the allograft itself may not be alone the reason for the high infection rate, but factors according to tumour treatment increasing the risk for infection. The extensive surgical procedure, sometimes multiple surgeries, the long duration of exposure, with often high loss of soft tissues, the amount of blood loss and the subsequent numbers of blood transfusions, as well as the effects of adjuvant chemotherapy and radiation and poor blood supply to the allograft are risk factors in developing an infection. (36, 80, 84, 92, 95, 115, 118, 122)

Many authors observed the trend that infections occur more often in patients receiving chemotherapy than in patients not receiving chemotherapy, but statistically significance could not be found because the number of cases was too low in the series. (73, 92, 95, 115, 122) Only Mnaymneh et al. could proof that chemotherapy increases the risk for infection statistically significant. (80) Mankin et al. found that infection rate in patients receiving chemotherapy alone (14%) did not differ greatly from the generally rate (12.8%), but radiation alone increased infections statistically to 38%. Likewise in patients receiving both chemotherapy and radiation the development of infection rose statistically to 21% showing that adjuvant treatment increases the risk of infection. (92)

Another risk factor for infection is a reconstruction in the proximal tibia. The proximal tibia is predisposed for infection, because of the insufficient soft tissue coverage.(13, 36) Adequate soft tissue coverage is essential to provide infection. Free or rotational muscle flaps are helpful to achieve good viable coverage of the allograft and to reduce the risk of infection thereby. (14, 83, 92, 117, 119, 122)

Since chemotherapy and radiation are essential for patient's survival, it is impossible to interfere in these points. To reduce infection it is important to reduce exposure and number of blood transfusions by performing the surgical procedure rapidly and under highest sterile conditions. (92) The most effective instrument to provide infection seems to be the use of free or rotational muscle flaps to assure adequate soft tissue coverage.

There also exists the hypothesis that infection as well as fracture and non union are immunologically directed as a form of rejection (14, 92, 95) (see also 1.3 Immunogenicity of bone allografts).

### 1.4.2 Fracture

Fracture is also a severe and common complication in allograft reconstructions with reported incidence from 0 to 54%. (13, 14, 29-31, 45, 63, 70, 71, 74-76, 80-82, 84, 85, 91, 107, 108, 116, 119, 125, 139-151) But although fracture has an adverse effect on final outcome, it is not that devastating as infection is. (14, 30, 33, 36, 71, 78, 81, 92, 93, 117, 151) Mankin et al., for example, observed a good or excellent result in 51% of fractured allografts compared with only 19% satisfactory results in infection (81) and Berrey reported results in fractured grafts after treatment similar to the non fractured group. (150) In a report of six allografts followed for 22 to 36 years, four of these allografts sustained an early fracture, but could be preserved and three achieved a good result demonstrating that even fractured grafts can survive for decades, if treatment is successful. (32) Although fracture often leads to failure of graft, these cases are also demonstrating that fractured grafts can recover and allografts have the potential to heal. Spontaneous healing is rare, mainly reported in non-weight bearing allografts (51, 75, 76) but also in lower limb. (13, 71, 80, 152) Sorger et al. found in all fractures which healed without surgical treatment, the fracture having close contact with host bone what provides better potential of healing. (71) Fracture healing took 4 to 24 months and therefore obviously longer than in normal bone fractures. (153) This is emphasised by Enneking's findings in retrieved allografts, where he found no callus formation or unusual internal repair but only ingrowth of fibrovascular repair tissue in grafts removed shortly after fracture. In grafts retrieved several months after fracture, however, increased internal repair and extensive revascularisation in region about fracture could be seen. (65) Surgical treatment of allograft fractures with open reduction, new internal fixation and autologous bone grafting is more common and more successful than cast immobilisation. Reported success rates of this treatment vary from 25% to 75%. (30, 32, 33, 36, 73, 78-80, 146, 151, 154) If bone grafting is not successful a vascularised fibula is another option to treat allograft fractures. With onlay of a vascularised fibula union excellent results are obtained and union can be achieved in most cases, but vascularised fibula transfer is technically demanding and donor side morbidity is not negligible. (30, 57, 58, 154) Although there are capable methods to achieve union not all fractured allografts can be salvaged, especially fractures through the shaft, without contact to living host bone, have limited intrinsic healing potential. But even if the allograft has to be removed limb salvage with another allograft or prosthesis is possible in almost all cases and good results are achieved. (30, 36, 71, 82, 117, 150, 155) Berrey (150) divided fractures into three groups and recommended adequate treatment for each type to achieve best results based on his findings on allografts. Type I he defined as rapid dissolution of the allograft which is rather an immune reaction and fortunately it is observed rarely. If a Type I fracture occurs, the graft has to be removed and reconstruction with a new allograft or another device can be done. A Type II fracture is a fracture of the shaft. This is the most common type of fracture and treatment should be done by open reduction, internal fixation and autologous bone grafting. In cases where the fracture has no contact to living host bone or when bone grafting was not successful a vascularised fibula should be used to achieve union. If all efforts are not leading to success the allograft must be removed and reconstruction with a new graft can be done. Type III fractures are characterised as fragmentation of joint, occurring in osteoarticular allografts. The optimal treatment for a Type III fracture is a conventional total joint replacement, if enough bone stock can be preserved. Removal of the allograft and reconstruction with either new osteoarticular allograft or tumour prosthesis is the alternative in fractured allografts without sufficient bone stock. (150)

The allograft is incorporated into the host bone by creeping substitution, meaning penetration of the graft by vessels, osteoclastic resorption of the allograft and substitution with host bone. This process is happening very slowly, superficially and only to a limited degree. Revascularisation and resorption compromise the mechanical integrity making the graft more susceptible for fracture, especially in two to three years after implantation, reflecting the domination of resorptive pattern during this time. Intense and rapid revascularisation increases the risk of fracture. (27, 30, 65, 67, 84, 119, 154) This conclusion is underlined by the fact that nearly all fractures are found within the first three years with and peak prevalence between 20 and 28 months after implantation of allografts. In most series no fracture without adequate trauma happened after 4 years from implantation indicating that the graft needs this time for revascularisation and sufficient remodelling to achieve endurable resistance to full weight bearing. (14, 27, 31, 36, 65, 70, 71, 78, 81, 150, 151, 154) Biopsies of fractures showed a lack of revascularisation and soft tissue attachment. During its life time the graft sustains microdamages and since the necrotic bone does not have the ability to remodel and repair itself, the allograft fractures of fatigue. Absence of revascularisation and host tissue ingrowth also increases the risk of fracture. (36, 67, 70) Cortical perforation improves revascularisation and bone incorporation, but since holes are stress risers and allografts are very sensitive to stress-concentrating defects this is even favouring a fracture instead of preventing it. (46, 68) There is a general consensus that everything creating a cortical defect should be avoided, because fracture occurs most commonly at screw holes or drill holes for tendon and ligament reattachment. (29, 46, 65, 70, 71, 78, 80, 84, 91, 93, 148, 151, 153, 154, 157)

To prevent fracture intramedullary fixation should been done, whenever possible. (65, 70, 154) It has been proven that an intramedullary device reduces considerably the fracture risk compared with fixation with plate and screws. (157) Intramedullary fixated allografts have lower fracture rates, because an intramedullary device is not destructing the cortical integrity by screw holes on the one hand and on the other hand supports the entire graft and increases its strength due to its load bearing and load sharing qualities. (4, 29, 41, 46, 71, 78, 158) This is also reflected in the fact that fracture rates are extremely low in allograft prosthesis composite reconstructions. Most fractures in APCs happened in cases where short stem prosthesis instead of long stem prosthesis bypassing the host-graft junction has been used. (30, 63, 107, 108, 142-144, 152, 159, 160)

Mechanical reinforcement of the allograft is also provided by cementing the allograft. (36) There are encouraging results with low fracture rates in series with cement filled allografts so that it seems that cementing strengthens the graft. (30, 161-163) The plate fixating the cement filled allograft – or an uncemented graft, when intramedullary fixation can not be done for any reason – should span the entire length of the graft for ideal support and to prevent fracture. (46,163) Parts of the allograft which are not protected by fixation device have in fact also a high risk to fracture since fractures at the end of plates or at the tip of a stem are common. (153,164) These observations lead to the conclusion that internal fixation protects the allograft and should be left in situ because removal would make the graft more susceptible to fracture again. (65, 78, 79)

Increased fracture rates where observed in irradiated allografts compared with fresh frozen allografts. Irradiation causes changes in structural characteristics of bone. It leads to a change in collagen crosslink which is important for biomechanical strength and modulus elasticity of bone. These changes weaken the graft so that nonirradiated allografts should be preferred. (29, 84, 147)

Chemotherapy favours also the occurrence of a fracture, with considerable higher fracture rates among patients receiving chemotherapy than among patients not receiving chemotherapy. This is probably related to prolonged union time and the consecutive prolonged instability at host-graft junction. (13, 84, 91) Sorger in contrast found that adjuvant therapy has no effect on fracture rate, but patients receiving chemotherapy had worse outcome after fracture than patients not receiving chemotherapy. (71)

A relationship between size of the allograft and fracture rate was also found as undersized allografts are more likely to fracture (25%) than allografts of the same

(15%) size or oversized grafts (13%), remembering that allografts should be matched in shape and size to achieve best results. (29)

A trend to increased fracture rates in allografts longer than 14 cm – this was the mean graft length in this series – was also observed, which turns up to be quite logical since longer allografts need prolonged time to incorporate and achieve stability. (153)

### 1.4.3 Nonunion

Nonunion is defined as the absence of radiographic signs of union one year after surgery. Some authors use delayed union synonymously, others distinguish non-union and delayed union, depending if union could finally be achieved or not. Per definition an allograft-host junction can be classified as nonunion not until a year, but treatment for non-union is generally done before and junctions are classified as nonunion anyway. (30, 84, 89, 140) Below non-union will be used if no signs of union are present after one year regardless if union can finally be achieved or not and/or if additional surgery was necessary to achieve union independent on the time at which revision was done.

Nonunion is probably the most prevalent allograft related complication with incidences reported up to 57%. (14, 27-30, 33, 41, 45, 51, 62, 74-81, 84, 89, 91-93, 104, 107, 108, 116, 117, 119, 120, 124-126, 140-146, 151-153, 157, 158, 160, 161, 163-172) Though nonunion occurs that often, it is the least devastating complication while it is the only one. Fox et al. (78) reported, that patients with no complication or nonunion had the best longterm results and Donati et al. (29) found good or excellent results in 64% of all nonunions. These observations are demonstrating that occurrence of nonunion has little or no adverse effect on final outcome. This is not a surprising observation since nonunion is the complication accounting for fewest failures, as achieving union is possible in most cases. In a series on 480 allografts Mankin et al. (14) found nonunion accounting for only 2.7% of all failures, really few compared with infection or fracture reasonable for 39% and 25%. (30, 33, 78, 81, 83, 84, 89, 93, 145, 153, 164)

Augmentation with autologous cancellous bone graft and – if necessary – realigning osteosynthesis device is the method of choice to treat nonunions and in a high number finally union can be achieved by this procedure. (27-30, 33, 41, 51, 62, 75, 77, 78, 80, 89, 93, 107, 115, 117, 119, 120, 141, 143, 144, 146, 152, 158, 160, 161, 163, 164, 166-168, 170, 172) In several cases bone grafting did not succeed union of allograft-host junction and further surgical procedures as a second bone grafting procedure or a vascularised fibula transfer to augment healing of allograft-host junction became necessary. (30, 33, 83, 163) The last has encouraging results, but the procedure is lengthy, technically demanding with regard to vascular dissection and reanastomosis and donor side complication is not negligible. (45, 57) Hornicek et al. (89) reported 17% persisting nonunions even after three or more surgical attempts to correct and 5% amputations due to concomitant infection or tumour recurrence. Outcome worsens with the number of additional procedures and, as mentioned above, grafts also fail to unite, especially if other complications like tumour recurrence, infection or fracture are concomitant. (30, 33, 79, 83, 84, 89, 91, 108, 117, 153, 160, 167) In very few reported cases the inability to achieve union did not even lead to failure of the graft since patients had no pain or other problems and refused further surgical treatment. (75, 163) Success rates after surgical treatment are high ranging from 58% to 100%. (33, 51, 78, 89, 117, 120, 157, 168)

Union of allograft-host junction is correlated to bone incorporation. If the living host bone has poor osteoinductive capacity, correction of a nonunion is difficult. (84, 89) To enhance bone incorporation, graft perforation was tried, as already mentioned above (see 1.4.2 fracture), but although more new bone was formed in the perforated grafts no difference in union could be found. (68)

Since augmentation of autogenic iliac crest bone grafts at the allograft-host junction achieves great results in treatment of nonunion, it would stand to reason to use autologous bone grafting at index procedure to prevent nonunion. But this discussed quite controversially in literature. (80, 115, 163) Some authors attribute their high union rates to initial bone grafting and recommend doing it, (104, 125, 161) while others found no different nonunion rates in graft-host junctions augmented with autologous corticocancellous bone compared to non augmented junctions and chose to desist from it. (29, 151, 157)

There are two principal determinants to achieve host-graft union: stability of construct and contact between host bone and allograft. (67) Vander Griend et al. (157) found a significant association between a problem in achievement of stable fixation and development of a nonunion. Other authors also observed that contact in osteotomic surfaces has a considerable influence on union, (29, 158) so that now there is a general consensus that a rigid internal fixation and close graft-host bone contact, avoiding any gaps, are necessary to prevent nonunion. (28, 46, 65, 67, 78, 80, 83, 84, 104, 151, 153, 166) Sufficient revascularisation providing blood supply and osteoblasts is also important to achieve union. (67, 151) Stevenson (67) found in his investigations on bone grafts in animals a lack of vessel proliferation only in unstable reconstructions, underlining the importance to create a stable construct.

No study could demonstrate, that type of fixation has an influence on nonunion rates, although close contact is more difficult to achieve with intramedullary device than with plates and some authors reported – probably for this reason – slightly higher non-union rates in allografts secured with intramedullary nails compared with plates and screws. (29, 33, 62, 83, 104, 120, 151, 154, 157, 158, 170, 172)

Cementing the allograft to reduce fracture risk seems not to compromise union. Though some authors found nonunions more frequent in cemented allografts than in uncemented, no significance could be proven and nonunion rates are not higher in APC reconstructions, which are generally cemented. Quite the contrary, their occurrence is even slightly lower, since cementing provides a very stable construct, but care has to be taken not to cover the graft-host bone interface with cement as this certainly leads to nonunion. (30, 115, 140, 161-163, 169)

Chemotherapy has an inhibitory effect on allograft union since cells at host-graft junction are under active proliferation and differentiation, making them more vulnerable to chemotherapeutic agents like cisplatin or other. This is expressed histologically in decreased osteoclastic resorption and diminished new-bone formation and clinical in increased non-union rates in patients receiving chemotherapy. Fortunately the suppression of osteoblastic activity by chemotherapy is a reversible process in humans with restoration of biological environment favourable to union at the end of a chemotherapeutic period. (29, 30, 33, 65, 80, 89, 91, 115, 151, 158, 160, 161, 165) This indicates that treatment to achieve union should be done after finishing chemotherapy protocols to get best results. (117, 166)

Postoperative radiation is also inhibiting union between host bone and allograft and nonunion rates are somewhat higher in patients receiving both chemotherapy and radiation. (29, 33, 67, 158, 165) In irradiated allografts - to eliminate microbial contamination - the occurrence of nonunion did not differ to non irradiated grafts, not a big surprise as union is initiated only by living host bone. (147)

In his series on retrieved allografts Enneking (65) made following observations in grafts removed due to nonunion: A varying amount of external callus spreads from host cortex but it is prevented to anneal to allograft by an envelope of fibrovascular tissue separating callus from the allograft. This kind of reactive capsule consists of richly vascularised tissue containing mononuclear leucocytes, occasional histiocytes and multinucleated giant cells, suggesting that non-union is probably a form of immune response. (14, 65, 69)

### 1.4.4 Joint instability

Joint instability is also often listed under the common complications in allograft reconstructions although it is a specific complication affecting only allograft constructs in which reconstruction of a joint is involved as osteoarticular allografts or allograft prosthetic composite reconstructions. (14) Reported instability rates vary from no unstable joints to an instability rate of 69%. (14, 30, 31, 41, 45, 51, 63, 74-78, 80, 81, 83, 91, 93, 108, 116, 117, 120, 121, 141-143, 145, 146, 148, 160, 166-168, 173, 174) Unstable joint are not as significant a problem as the triad of infection, fracture and non-union. Unstable joints rarely end in failures and in general they do not compromise final results, with most patients achieving satisfying results (excellent or good). (14, 51, 81, 93, 104, 117, 145, 146) A considerable number of patients with unstable joints can be treated conservatively reducing risks coming along with additional surgical procedures. (31, 51, 91, 104, 142) Mankin (14) found among 104 failed allografts only four with joint instability reasonable for removal of the graft. There are several treatment options for joint instability depending on the type of initial reconstruction, the affected joint and severity of instability. Especially in reconstructions involving the knee instability can be handled well with braces. (31, 80, 91, 93) In osteoarticular reconstructions a conversion to a total joint arthroplasty is often done to improve stability. (82, 91, 93) Arthrodesis achieves good results in treatment of radiocarpal instability and distal radioulnar joint instability occurring after reconstruction of the distal radius with an osteoarticular allograft as well as for unstable shoulders as a consequence of proximal humerus reconstruction done with either an osteoarticular allograft or an allograft prosthesis composite. (77, 146) In dislocations of the hip after APC reconstruction of the proximal femur closed reduction is possible in most cases and only few necessitate open reduction. (120, 167, 173) Most reported dislocations were a single event and only Anract (122) reported that he had to revise acetabular component to a constrained cup in a patient who sustained multiple dislocations.

In osteoarticular allografts ligamentous instability is generally caused by less than optimal reconstructions with anatomical incongruity. Size mismatch and consecutive joint instability cause joint detoriation and degenerative arthritis, emphasising the importance of best possible size match and soft tissue repair. (80, 82)

Joint instability is rather related to tumour resection and the considerable loss of soft tissue than to the allograft itself. (74, 121, 148) Highest instability rates are reported in proximal humerus reconstructions. (63, 93, 142, 144, 148) The shoulder joint is primarily stabilized by the muscles of rotator cuff, so it is not astonishing that a loss of rotator cuff due to tumour resection leads to instability. A careful soft tissue balancing of rotator cuff tendons and glenohumeral capsule is the best aid to minimize the risk of glenohumeral instability. (160) Not only in shoulder reconstructions but also in all joint reconstructions careful soft tissue reconstruction should be done to prevent any instability. (80, 82, 108, 120)

Distal radioulnar joint instability and consecutive radiocarpal instability are quite common in distal radial osteoarticular allografts. In most cases DRUJ instability generates only mild symptoms and only few require an arthrodesis. (75, 77, 116)

Szabo (76) used the Sauve-Kapandji procedure – arthrodesis of distal radioulnar joint and ulna shaft osteotomy – in his series on osteoarticular allograft reconstructions of distal radius. No joint instability occurred after this procedure suggesting that the Sauve-Kapandji procedure is a good method to prevent DRUJ instability.

# 2 Special part

## 2.1 Aim

In limb-sparing treatment of bone tumours, biological reconstruction with a bone graft (autogenic or allogenic) or endoprosthetic reconstruction, are generally the alternatives to handle large bony defects after wide resection. As a result of multimodal therapy concept combining polychemotherapy with wide resection and when indicated additional radiation, sarcoma patients are now having a considerable improved prognosis. (15-23, 45, 175, 176) Since patients now have a good chance to outlive their disease reconstruction's durability as well as complications and their consequences must be taken into consideration to choose the appropriate reconstruction method.

It is the aim of this diploma thesis to work out how long allograft reconstructions last as well as to work out the complications compromising the outcome and their frequencies. This will be done with a special regard to reconstruction types also performed at the Department of Orthopaedic Surgery Graz.

## 2.2 Material and Methods

Two things were done to answer the questions about durability and complications of allograft reconstructions.

First all patients at the Department of Orthopaedic Surgery Graz who received an allograft for reconstruction of a skeletal defect following tumour resection were identified. Two groups with sufficient data for an adequate retrospective analysis were determined, one group with intercalary allografts augmented by autologous vascularised fibula for reconstruction of tibial or femoral defects and the other one with osteoarticular allograft reconstructions of the distal radius. As the numbers of patients in both groups were too small to make general statements and no sufficient data for evaluation of the other types of allograft reconstruction – also performed at the Department of Orthopaedic Surgery Graz– were available, an additional literature review was done to get more information. Literature was reviewed for the both reconstruction types mentioned above as well as for massive intercalary allografts alone and intercalary prostheses as alternatives to a vascularised fibula with an allograft shell. Further the literature was sifted through for studies about allograft prosthesis composite reconstructions of the proximal humerus and of the proximal femur, since these types of allograft reconstructions were also performed at the Department of Orthopaedic Surgery Graz. Additional literature was examined for published data about osteoarticular allografts around the knee as distal femur and proximal tibia are the most common locations for bone tumours.

### 2.2.1 Vascularised fibula combined with a massive allograft shell

Fourteen patients (4 male, 10 female) were identified who received an autologous vascularised fibula for reconstructions of tibial or femoral defects at the Department of Orthopaedic Surgery Graz. Twelve of the fibula reconstructions were combined with a massive allograft and two were done without allograft supplementation. In all respects the two reconstructions without an allograft were no outliners and therefore they were not excluded. Patients‘ medical records were scanned for following data: age at operation, length of follow-up, pathology and localisation of the tumour, additive treatment with chemotherapy or radiation, length of bone defect, fixation device, operating time, time to partial and full weight bearing, occurrence of complications due to the allograft with a special regard to infection, fracture and non-union, as well as complications due to the tumour (local recurrence, distant metastases, dead of disease), revision procedures and failure of the reconstruction. Failure of the reconstruction was defined as removal of the construct for any reason.

Descriptive statistics were calculated using means and proportions depending on the type of data. The survival rates of patients as well as of reconstruction were estimated using the Kaplan-Meier method. Log-rank test was used to compare survival curves. Pearson's chi-square test and two tailed Fisher's exact test were used to identify correlations.

### 2.2.2 Osteoarticular allograft reconstructions of distal radius

Most data of the patients group with osteoarticular allografts for distal radius were already evaluated for a paper about giant cell tumours by a senior house officer at the Department of Orthopaedic Surgery Graz, who kindly provided these for this thesis. To this data of patients with osteoarticular allograft reconstructions of distal radius and other diagnoses than giant cell tumour were added. Age at operation, length of follow-up, resection length, type and frequencies of complications (related to both allograft and tumour) and revision procedures were determined from patients' records. The Mayo wrist score and the DASH score were used to evaluate functional outcome. Mayo wrist score is an objective evaluation of function by comparing range of motion with the healthy side and examining grip strength and pain. A maximum score of 100 points is attainable and results are classified as excellent (91-100), good (80-90), fair (65-79) and poor (below 65). The DASH score measures general function in daily life by 30 items scored from 1 to 5 with 1 standing for no disability and 5 for maximum disability. The end score is converted to a scale from 0-100 where 0 implies no disability and 100 maximum disability.

Statistical analysis was done using descriptive methods as means and proportions appropriate to type of data. Survival rates were estimated using the Kaplan-Meier method.

### 2.2.3 Literature review

The PubMed database was browsed for papers on allograft reconstructions after bone tumour resection with special regard to following types of reconstruction: intercalary allograft reconstructions for femoral and tibial defects with and without supplemental vascularised fibula, osteoarticular allograft reconstructions of distal radius and such around the knee as well as allograft prosthesis composite reconstructions of proximal humerus and of proximal femur. Additional articles about the use of intercalary prosthesis were searched as an alternative to allografts. To cover articles – eventually undetected by used search strategies – cross-referencing was done. The outcome of this research was reviewed with regard to outcomes, complications and survival rates.

## 2.3 Results

### 2.3.1 Intercalary reconstruction with an autologous vascularised fibula combined with an allograft shell

#### *2.3.1.1 Own study results*

**Patients and reconstructions**

14 patients received an autologous vascularised fibula to reconstruct a segmental defect after tumour resection with a mean follow-up of 41.5 months (median: 37.8; range: 2-88 months). There were ten female and four male patients with a mean age of 20.6 years (median 16.2; range: 11-57; fig 2.1). Seven tumours were located in the femur and seven in the tibia. Primary diagnoses are distributed as

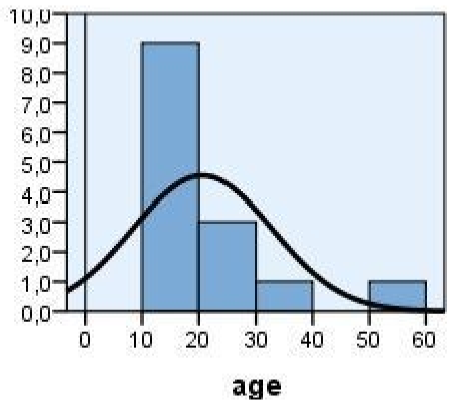


*Figure 2.1: Distribution of patients' age.*

followed, six Ewing's sarcoma, five osteosarcoma, two liposarcoma (one G2 and one G3) and one adamatinoma. Four patients received no additive tumour treatment, seven received chemotherapy, two chemotherapy and radiation and one received only radiation.

Twelve fibula reconstructions were combined with a massive allograft and two without a supplemental allograft shell. In two patients the graft-host junctions were augmented with autologous cancellous bone grafts at the index surgery while twelve had no additional bone grafting. The length of bone defect was 17.6 centimetres on mean (median: 18 cm; range 8.5-25 cm) and surgical procedure lasted 217 minutes on average (median: 129; range 86-723).

**Oncologic results**

At time of writing this thesis ten patients were alive without evidence of disease. None of the 14 patients forming this study group had a local recurrence. Three developed distant metastases in lung and – despite treatment with metastasectomy and chemotherapy – died of their disease.

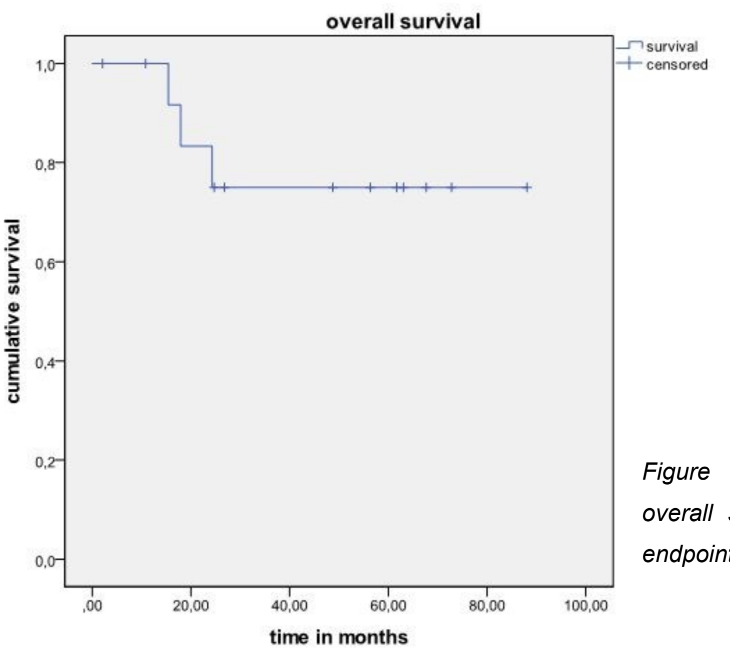


*Figure 2.2: Kaplan-Maier curve for patients' overall survival rate with dead of disease as endpoint.*

One patient was alive with evidence of disease, after primary occurrence of lung metastases a metastasectomy was performed but metastases recurred. The overall survival rate with dead of disease as endpoint was 83.3% at two years and 75% at three and five years (fig 2.2).

**Graft survival and complications**

None of the grafts was removed. All patients achieved full weight bearing without support of braces, crutches or a cane (fig 2.6). Partial weight bearing was allowed at two months after operation on average (median: 1.7; range: 1.4 – 4.6 months) and full weight bearing at a mean of 8.9 months postoperative (median: 7.9; range: 3.7 – 27.6). The patient who achieved full weight bearing not until 27.6 months had a nonunion and sustained a fracture both protracting time to full weight bearing.

Six patients had 14 additional surgical interventions for complication management. This is a mean of one (range 0-6) additional surgical procedure at 10.8 months on average after primary surgery. The event free survival rate (fig 2.3) with event as any complication requiring an additional surgical intervention was 69.6% at two years and 49.7% at three and five years.

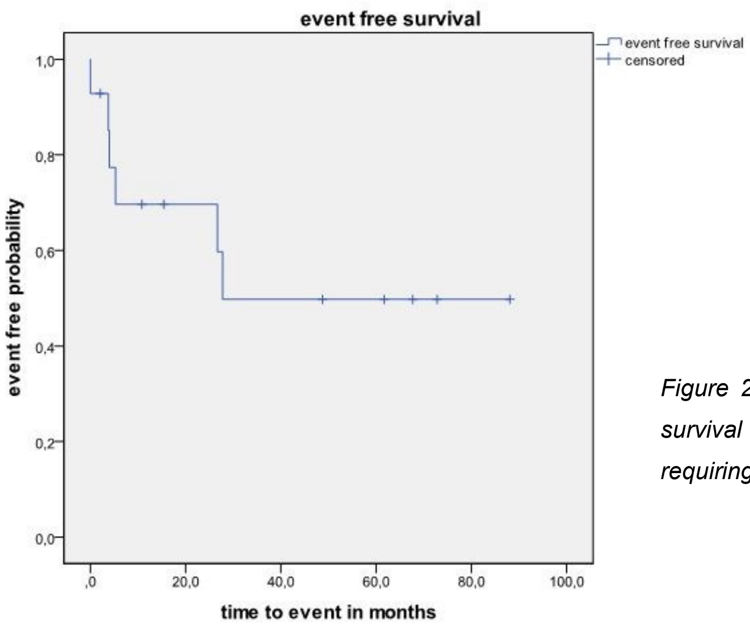


*Figure 2.3: Kaplan-Maier curve for event free survival with event defined as any complication requiring additive surgical intervention.*

Event free probabilities for patients receiving additive treatment with chemotherapy and/or radiation are similar to those of patients without additive treatment (fig.2.4): 75% at two years and 50% at three and five years for patients with additive treatment and 67.5% at two years and 50.5% at three and five years for patients without (p-value: 0.968). Also chemotherapy or radiation alone had no influence on event free probability (p-values: 0.744 and 0.678).

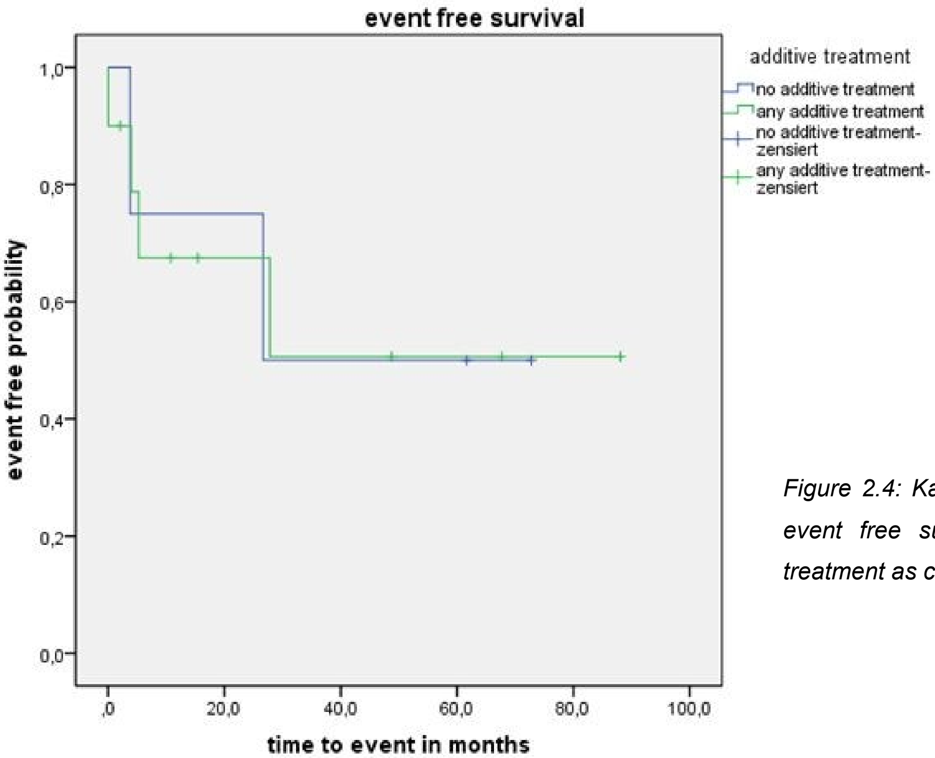


*Figure 2.4: Kaplan-Maier curve for event free survival with additive treatment as compromising factor*

Eight patients had 13 local complications. In four patients, all with femoral reconstructions, the plate had broken leading to subsequent fracture of the graft (fig. 2.6). One patient fell because one of his crutches was broken which resulted in plate breakage and graft fracture. The other three patients sustained plate breakage without adequate trauma. All four were successfully treated with open reduction, replacement of internal fixation and autologous iliac cancellous bone grafts were augmented around the fracture. Only a reconstruction of the femur could be identified as risk factor for fracture. 57% of all femoral reconstructions fractured while no tibial reconstruction sustained a fracture (p = 0,018 Pearson's chi-square, p = 0,035 Fisher's exact test two tailed). No correlation could be found between fracture and the length of bone defect, time to partial weight bearing or time to full weight bearing.


***a)*** ***b)*** ***c)*** ***d)*** ***e)***

*Figure 2.5: Liposarcoma G2 of the femur, female, 31 years* ***a)*** *x-ray preoperative* ***b)*** *MRT preoperative* ***c)*** *1 week postoperative* ***d)*** *plate breakage and fracture 15 months postoperative* ***e)*** *1 month after revision*

Three patients had a nonunion, two of them were successfully treated with ESWT (Extracorporeal Shock Wave Therapy) and one healed without further intervention after 18 months. Wound healing disorders occurred in three patients, all in tibial reconstructions and could be treated with debridement, vacuum assisted wound closure (necessary in one patient) and consecutive wound coverage. One of the patients with wound healing disorder developed deep infection which was successfully managed with removal of internal device and systemic antibiotics. Another patient also sustained infection but unfortunately he died because of progressive disease before treatment of infection could be started. Haematoma requiring surgical intervention occurred in one patient.

***2.6 a)*** ***2.6 b)*** ***2.6 c)***

*Figure 2.6: Adamantinoma of the tibia; female, 24 years Reconstruction with vascularised fibula and allograft*

***a)*** *X-ray preoperative,* ***b)*** *X-ray 3 months postoperative,* ***c)*** *X-ray 4 years postoprative*

A trend could be identified that tibial reconstructions favours wound healing disorders, since all occurred in tibial reconstructions but in the low number of patients statistically only a trend could be detected (p = 0.053 Pearson's chi-square). No correlation could be demonstrated between additive treatment in any form and the occurrence of local complications.

Three patients had four donor side complications. All three had flexion deformity of the big toe and one had additional claw toes.

### *2.3.1.2 Literature review*

Results of literature review are summarised in table 2.1 and table 2.2. Graft survival rates are ranging between 80% and 100% at a reported follow-up of 3 to 10 years. El-Gammal et al. (49) reported only the low (patients') survival rate of 53% in 16 high grade sarcomas but no graft failures were mentioned. Local complications are quite frequent and up to 50% of all reconstructions require at least one additional surgical intervention. But despite these high complication and revision rates it is mostly possible to get a handle on complications. The fact that complications are successfully manageable is reflected in the low failure rates and the good functional outcomes (see table 2.1). The most common local complication is fracture with incidence up to 36%. Infection rates ranged from 0 to 29% and nonunions occurred in up to 31% of all reconstructions. (49, 177-187)

Union at the fibula host junction occurred around 5 months and at the allograft host junction 11 to 20 months were needed to achieve union. Full weight bearing was allowed quite differently between 6 and 20 months after primary surgery. (49, 177-187)

A disadvantage in the use of vascularised autografts is donor side morbidity, which is reported with quite different frequencies. Most recorded complications due to harvest of the fibula are minor complications not really compromising the outcome. The most common donor side complication is flexion deformity of the big toe which is observed by nearly all authors. (49, 177-187)

| author | Capanna R. et al. | Li J. et al. | Jager T. et al. | Li J. et al. | Yang Y.F. et al. | Innocenti M. et al. |
|---|---|---|---|---|---|---|
| journal & year | Orthop Clin N Am 2007 | J Surg Oncol 2010 | Orthopaedics & Traumatology 2010 | J Reconstr Microsurg 2010 | J Reconstr Microsurg 2010 | Microsurgery 2009 |
| patients [n] | 90 | 11 | 7 | 8 | 17 | 21 |
| age [years] | n.s | 18,5 (11;32) | 12 (8,5;17) | 16,5 (11;28) | 18,4 (6;34) | 18,1 (5;52) |
| follow-up [mo] | 108 (36;204) | 34,1 (17;53) | 44,1 (36;63) | 38,4 (17;58) | 20,2 (6;48) | 139,3 (28;213) |
| CTX/RTX [n] | n.s | 8/1 | n.s | 6/0 | n.s | 15/0 |
| local recurrence | 7 | 2 | n.s | 1 | 1 | 2 |
| DOD | n.s | 1 | n.s | 1 | 0 | 1 |
| fibula with allograft [n] | 90 | 11 | 7 | 8 | 17 | 21 |
| fibula alone [n] | 0 | 0 | 0 | 0 | 0 | 0 |
| tibia [n] | 57 | 6 | 3 | 8 | 9 | 21 |
| femur [n] | 33 | 5 | 4 | 0 | 8 | 0 |
| lenght of defect [cm] | 16 (7;26) | 12,1 (9;16) | 17,6 (13,5;22) | 11,8 (9;16) | 16,6 (12;25) | 15,3 (7;26) |
| lenght of fibula [cm] | n.s | 16,2 (12;20) | n.s | 15,9 (12;20) | 18,3 (15;28) | 18,8 (12;28 |
| op-time [h] | n.s | 6 (4,3;7,6) | 10,3 (8,2;13) | 5,6 (4,3;7,6) | n.s | 7,7 (6;12) |
| full weight bearing [after mo] | n.s | 12,4 (9;16) | 5,4 (3;8) | 14,7 (11;20) | n.s | 21,6 (14;36) |
| union fibula-host [mo] | n.s | 5,4 (4,5;7,5) | 7 (3;24) | 5,8 (5;8) | 13 in 6 months; 3 in 8 months | 5,4 (3;10) |
| union allograft-host [mo] | n.s | 11,8 (8;15) | | 14,1 (12;17) | | 19,1 (10;34) |
| complications donor site | n.s | 10 in 5 pat | 7 in 6 pat | 4 in 2 pat | 0 | 5 in 4 pat |
| infection [n] | 7 (7,5%) | 0 | 1 (14,28%) | 0 | n.s | 1 (4,7%) |
| fracture [n] | 12 (13,3%) | 0 | 1(14,28%) | 0 | n.s | 6 (28,5%) |
| nonunion [n] | 8 (8,8%) | 1 (9%) | 2 (28,5%) | 2 (25%) | n.s | 2 (9,5%) |
| revision procedures | 25 had ~1 add op | 2 had 1 add op | 3 had 1,3 add op | 3 had 1 add op | 5 | 7 had 1,9 add op |
| failure [n] | 6 (6,5%) | 1 (9%) | 0 | 1 (12,5%) | 1 (5,9%) | 4 (19%) |
| reconstruction survival | 93,3% at ~9 years | 90,9 % at ~2,8 years | 100% at ~3,7 years | 87,5% at ~3,2 years | 94% at ~1,7 years | 80,9% at 10 years |
| function [[1] MSTS; [2] Mankin score] | 72% excellent; 20% good; 5%fair; 3% poor [1] | 91,8%[1] | n.s | 90,8%[1] | 8 excellent; 5 good; 2 fair; 2 poor[2] | 91% (60;100)[1] |

*Table 2.1: Literature review about intercalary allograft reconstructions combined with an autologous vascularised fibula part 1*

| author | Abed Y.Y. et al. | Moran S.L. et al. | Bernd L.et al. | Hennen J. et al. | El-Gammal T.A. et al. | Ozaki T. et al. |
|---|---|---|---|---|---|---|
| journal & year | JBJS Br 2009 | PRS 2006 | Orthopäde 2003 | Unfallchirurg 2002 | Microsurgery 2002 | Acta Orthop Scand 1997 |
| patients [n] | 25 | 7 | 16 | 10 | 25 | 12 |
| age [years] | 19,7 (5;52) | 10,5 (5;18) | 23 (7;53) | 30,8 (7:65) | 23,5 (11;50) | 14 (7;54) |
| follow-up [mo] | 140 (28;213) | 52 (24;84) | 60,38 (17;180) | 31,12 (14;56) | min 24 months | 32 (24;42) |
| CTX/RTX [n] | 18/0 | 4/0 | n.s | 6/1 | 16/n.s | 10/6 |
| local recurrence | 2 | n.s | 0 | 2 | 4 | 1 |
| DOD | 1 | n.s | 0 | 0 | 6 | 0 |
| fibula with allograft [n] | 25 | 7 | 11 | 10 | 0 | 12 |
| fibula alone [n] | 0 | 0 | 5 | 0 | 25 | 0 |
| tibia [n] | 21 | 4 | 3 | 3 | n.s | 12 |
| femur [n] | 4 | 3 | 13 | 7 | n.s | 0 |
| lenght of defect [cm] | 13,5 (10;26) | 13 (5;17,5) | 17,1 (9;29,5) | 15,8 (9;28,5) | 16 (9;20) | 14 (8;24) |
| lenght of fibula [cm] | 18,9 (12;28) | 20,2 | n.s | n.s | n.s | n.s |
| op-time [h] | 8,5 (6;12) | n.s | n.s | n.s | n.s | n.s |
| full weight bearing [after mo] | 21,4 (14;36) | n.s | n.s | 12,3 (8;14) | 7,5 (5;14) | 9 |
| union fibula-host [mo] | 5,6 (3;10) | 4 | n.s | 17 (12;24) | 4,5 (3;8) | n.s |
| union allograft-host [mo] | 19,6 (10;34 | 9 | n.s | | n.a | n.s |
| complications donor site | 6 in 5 pat | 1 in 1 pat | 1 in 1 pat | 0 | 6 | n.s |
| infection [n] | 1 (4%) | 0 | 2 (12,5%) | 1 (10%) | 1 | 0 |
| fracture [n] | 9 (36%) | 2 (28,6%) | 1 (6,25%) | 0 | 3 | 4 (33%) |
| nonunion [n] | 1 (4%) | 2 (28,5%) | 5 (31,3%) | 1 (10%) | 2 | n.s |
| revision procedures | 9 had 1,5 add op | 6 | 6 had 1,5 add op | 5 | 13 | 6 had 1,8 add op |
| failure [n] | 5 (20%) | 0 | 1 (6,3%) | 2 (20%) | n.s | 0 |
| reconstruction survival | 79% at 5 years | 100 % at ~4,3 years | 93,75 % at ~5 years | 80% at ~2,6 years | (53% at 3 years) * | 100% at ~2,6 years |
| function [[1] MSTS; [2] Mankin score] | 91,3% (60;100)[1] | 4 excellent; 3 good[2] | 93% (43;100)[1] | 73,3% (46;90)[1] | 78,7% (23;93)[1] | 5 excellent; 7 good[1] |

*Table 2.2: Literature review about intercalary allograft reconstructions combined with an autologous vascularised fibula part 2; *in 16 high grade sarcomas*

### 2.3.2 Intercalary allograft reconstructions

Results of the review about intercalary allograft reconstructions are summarised in table 2.3 and table 2.4. Reconstruction survival ranges between 70% and 92% at 5 years and between 53% and 84% at 10 years. As expected most frequently reported complications were fracture, infection and nonunion. Fracture rates varied from 0 to 34% with Alman et al. as only one outliner, who observed fracture in five of six intercalary allografts. Infection was recorded in up to 20% of allograft reconstructions. With incidences up to 46% nonunion seems to be the most frequent complication in intercalary allografts.

Complications were frequent but manageable and even if the graft failed limb could be preserved in most cases. Amputation was only necessary in a few numbers of reconstructions (0-17%) with mostly local recurrence as indication and their incidence was reported from no local recurrence to 18%.

Despite complications the reported functional outcome after intercalary allograft reconstruction is generally good (see table 2.3 and table 2.4). (27, 28, 32, 33, 62, 149, 153, 158, 163, 164, 172, 188)

| authors | Zimel M.N. et al. | Muscolo D.L. et al. | Muscolo D.L. et al. | Ortiz-Cruz E. et al. | Deijkers R.L.M. et al. | Chen T.H. et al. |
|---|---|---|---|---|---|---|
| journal&year | CORR 2009 | JBJS Am 2004 | CORR 2004 | JBJS Am 1997 | CORR 2005 | JBJS Br 2005 |
| patients [n] | 38 | 13 | 59 | 104** | 35 | 13 |
| age [years] | 16,3 (4,4;45,3) | 18 (9;40) | 28 (4;66) | 28,3 (4;69)** | 24 (11;68) | 31,3 (12;74) |
| follow-up [months] | 105 (14;231) | 63 (24;144) | 60 (24;264) | 73 (24;220)** | 86,4 (22;168) | 66 (24;130) |
| CTX/RTX | 34/2 | 13/n.s | 35/n.s | n.s | n.s | 13/n.s |
| femur [n] | 38 | 8 | 40 | 39 | 22 | 10 |
| tibia [n] | 0 | 5 | 19 | 38 | 13 | 3 |
| allograft lenght [cm] | 15,3 (6,5;31,7) | n.s | n.s | 16<10cm,59 10-18cm,29>18cm** | 14,5 (9;28) | 16,7 (10,3;26,1) |
| local recurrence [n] | 7 | 1 | 6 | 4** | 4 | 1 |
| DOD [n] | 8 | 1 | 5 (7%) | 8** | 11 | 2 |
| fracture [n] | 1 (2,6%) | 3 (23%) | 4 | 18 (17%)** | 12 (34,3%) | 2 (15,4%) |
| infection [n] | 7 (18,4%) | 1 (7,8%) | 3 (5%) | 12 (12%)** | 3 (8,6%) | 0 |
| nonunion [n] | 6 (15,8%) | 2 (15,4%) | 9 (15,3%) | 31 (30%)** | 10 (28,6%) | 6 (46,2%) |
| amputations [n] | 6 | 0 | 0 | 8** | 0 | 1 |
| grafts failed [n] | 15 (39,5%) | 4 (30,8%) | 9 (15,3%) | 15 (14,4%)** | 6 (17%) | 1 (7,7%) |
| function [[1]Mankin score; [2]MSTS 1987; [3]MSTS 1993] | n.s | 27 (10;30) [3] | n.s | 51 exc., 36 good, 2 fair, 15 failure**[1] | 23,5 (16;30)[3] | 86% (80;93)[3] |
| graft survival rate at 5y/10y [%] | 70/53 | 69,2% at 5,25 years | 79/-- | --/84** | --/79 | 92,3% at 5,5 years |

*Table 2.3: Literature review about intercalary allografts part 1; range and percentage in round braces; ** including intercalary allograft reconstructions at other locations than femur and tibia*

| authors | Miller B.J. et al.* | Ramseier L.E. et al.* | Gerrand C.H. et al.* | Alman B.A. et al.* | Cara J.A. et al.* | Muscolo D.L. et al.* |
|---|---|---|---|---|---|---|
| journal&year | CORR 2010 | JBJS Br 2006 | J Surgical Oncology 2003 | JBJS Am 1995 | Acta Orthop Scand 1994 | JBJS 1992 |
| patients [n] | 3 {8} | 5 {21} | 11 {45} | 6 {26} | 25 {26} | 2 {6} |
| age [years] | 35 (24;42) | 8 (7;12) | 46 (15;47) | 11,08 (5;15) | 16 (5;48) | 20 (16;24) |
| follow-up [months] | {18 (3;39)} | 41,4 (22;73) | 42 (8;97) | 54,8(44;75) | 36(12;72) | 288 (264;312) |
| CTX/RTX | 0/1 | n.s | 3/3 | n.s | 26/26 | n.s |
| femur [n] | 3 | 0 | 5 | 3 | 17 | 2 |
| tibia [n] | 0 | 5 | 6 | 3 | 8 | 0 |
| allograft lenght [cm] | {16,9 (7;30)} | n.s | {15 (6;29)} | n.s | 20 (10;32) | n.s |
| local recurrence [n] | 1 | 0 {1} | 0 {3} | 0 {1} | 3 {3} | 0 |
| DOD [n] | 1 | 0 {5} | 6 {17} | 0 {4} | 2 {2} | 0 |
| fracture [n] | 0 | 0 {6} | 0 {4} | 5 (83,3%) {14} | 2 (8%) {2} | 2 {4} |
| infection [n] | 0 | 1 (20%) {2} | 2 (18,2%) {4} | 1 (16,7%) {3} | 4 (16%) {4} | 0 {0} |
| nonunion [n] | {2} | 0 | 2 (18,2%) {8} | 1 (16,7%) {4} | 6 (24%) {6} | 0 {0} |
| amputations [n] | 0 | 0 {1} | 0 {3} | 1 {3} | 1 {1} | 0 {0} |
| grafts failed [n] | 0 | 0 {8} | 1 (9%) {4} | 1 (16,7%) {4} | 3 (12%) {3} | 0 {0} |
| function [[1]Mankin score; [2]MSTS 1987; [3]MSTS 1993] | n.s | 3 excellent; 2 good[1] | 84,3% ** [2] | 4 exc, 1 fair, 1 failure[1] | 9 excellent; 5 good; 4 fair;4poor[2] | 100% {82%}[2] |
| graft survival rate at 5y/10y [%] | 100% at 1,5 years | 100% at 3,5 years | {86/--} | 83,3% at 4,6 years | 88% at 3 years | n.s |

*Table 2.4: Literature review about intercalary allografts part 2; range and percentage in round braces; * number of total series in curly brackets, including patients with other allograft types; ** including intercalary allograft reconstructions at other locations than femur and tibia*

### 2.3.3 Intercalary prostheses

| author | Hanna S.A.et al. | Ruggieri P. et al. | Abudu A. et al. | Aldlyami E. et al. | Ahlmann E.R. et al. |
|---|---|---|---|---|---|
| journal, year | JBJS Br 2010 | J Surg Oncol 2011 | JBJS Br 1996 | Int Orthop 2005 | JBJS Br 2006 |
| type of prosthesis | custom made | modular system Osteobridge IDSF | custom made | custom made | custom made |
| diagnosis | primary sarcoma | primary sarcoma and metastatic disease | primary sarcoma | primary sarcoma | primary sarcoma and metastatic disease |
| patients [n] | 28 | 24 | 18 | 35 | 6 |
| femur [n] | 28 | 11 | 13 | 29 | 2 |
| tibia [n] | 0 | 8 | 3 | 3 | 3 |
| humerus [n] | 0 | 5 | 2 | 3 | 1 |
| age [years] | 41,3 (10;68) | 62 (40;78) | 26 (9;64) | 29 (8,75) | 42 (28;64) |
| follow up [months] | 97(3;240) | 29 (6;51) | 66 (6;188) | 107 (24;3069 | 21,6 (9;58) |
| bone defect [cm] | n.s | 10 (4;15) | 21 (16;28) | 19 (10;27,6) | 12,3 (8;16) |
| survival of implant | 85% at 5y and 68% at 10y | n.s | n.s | 63% at 10y | 100% at 1y, 83% at 2y |
| infection [%] (F/T/H [n]) | 3,6% (1/0/0) | 0 | 0 | 2,9% (0/1/0) | 0 |
| prosthetic fracture [%] (F/T/H [n]) | 7,1% (2/0/0) | 4,2%(1/0/0) | 0 | 5,7% | 0 |
| periprostehtic fracture [%] | 3,60% | 0 | 0 | 2,90% | 0 |
| aseptic loosening [%] (F/T/H[n]) | 3,6% (1/0/0) | 25% (4/1/1) | 33% (3/1/2) | 20% (5/1/1) | 16,7% (0/0/1) |
| function [MSTS] | 87% (67;93) | upper extremity: 90% (87;95), lower extremity: 86% (70;95) | femoral: 83,5%; tibial: 86,5%; humeral: 70 and 77% | n.s | 27 (25;28)* |

*Table 2.5: Literature review about intercalary prostheses; range and percentage in round braces F =femur; T = tibia; H = humerus; * max. score = 30*

Intercalary prostheses are an alternative to allograft reconstructions, but only a few reports about this reconstruction method could be found in literature. The results of this review are summarised in table 2.5.

Hanna et al. reported an implant survival rate of 85% at five years and 68% at ten years, Aldlyami et al. found similar 63% surviving reconstructions at ten and Ahlmann et al. observed only 83% implant survival at two years. The most common complication with intercalary prostheses is aseptic loosening with incidences ranging from 3.6% to 33%. Other collective complications are infection, with incidences from 0 to 3.6%, prosthetic fracture with rates ranging from o to 7.1% and periprosthetic fractures (0 to 3.6%).

Overall reported functional outcome after reconstruction with an intercalary prosthesis is good. (131-135)

### 2.3.4 Osteoarticular allograft reconstruction of distal radius

#### *2.3.4.1 Own study results*

From 2000 to 2011 six patients received an osteoarticular allograft reconstruction of distal radius with a mean follow up of 32 months (range: 3.7-121). There were five female and one male patient with a mean age of 42 years (range 22-64). Five reconstructions followed en bloc resection of a giant cell tumour and one was done after wide resection of an osteosarcoma. Two patients with giant cell tumour were primarily treated with curettage and polymethylmetacrylate filling but they experienced local recurrence and an en bloc resection and reconstruction with an osteoarticular allograft was performed. In three of the six patients the dominant limb was affected. The mean bone resection length was 6.5 centimeters (range: 5-11.5).

None of the patients sustained local recurrence or distant metastases after tumour resection and allograft reconstruction. At the last follow up all six allografts were fully functional and had survived (fig.2.7). Two patients developed nonunion at the allograft-host junction, which were successfully treated with autologous bone grafting. There were no infections, fractures or fixation failures.

*a) b) c) d)*

*Figure 2.7: Giant cell tumour of distal radius ,female, 45 years* ***a)*** *preoperative x-ray ap* ***b)*** *preoperative x-ray lateral* ***c)*** *reconstruction with an osteoarticular allograft 4 years postoperative ap* ***d)*** *the same lateral*

None of the patients expressed pain and everyone returned to prior work. The mean flexion/extension was 38/60 degree and the mean pronation/supination was 77/76.7 degree. The mean outcome of the Mayo wrist score was 84 and for DASH score the mean result was 7.7, both representing a good functional result.

### *2.3.4.2 Literature review*

Results of literature review are summarised and compared with our own results in table 2.6 and table 2.7. Survival rates of osteoarticular allograft reconstructions for distal radius are reported up to 100% at round about 5 years. With longer follow up reconstruction survival diminished a little. Kocher et al. recorded 66% survival rate at 10.9 years and Harness et al. noted 73.3% graft survival at 19 years.

Frequent complications in osteoarticular allografts at this side are joint instability with incidences recorded up to 100% and nonunion with rates ranging from 0 to 40%. Fracture occurred with incidences varying from 0 to 25%. Infection rates are surprisingly low as only Szabo et al. reported one minor postoperative infection and no deep infection was reported in literature.

Functional outcome was generally reported as good with satisfying range of motion, see also table three for a comparison of reported ranges of flexion/extension and pronation/supination. (75-77, 116, 124-127, 168)

| | MUG | Scoccianti G. et al. | Szabo R.M. et al. | Bianchi G. et al. | Kocher M.S. et al. |
|---|---|---|---|---|---|
| journal&year | | JBJS Br 2010 | J Hand Surg Am 2006 | J Hand Surg Br 2005 | JBJS Am 1998 |
| patients [n] | 5 | 17 | 9 | 12 | 24 |
| dominant hand [n] | 3 | 8 | 5 | n.s 8R/4L | n.s 17R/7L |
| age [years] | 42 (22;64) | 36,6 (13;56) | 42 (21;83) | 28 (13;65) | 31,5 (15;61) |
| follow up [months] | 32 (3,7;121) | 58,9 (28;119) | 100 (39;219) | 52 (26;145) | 130,8 (25;268) |
| resection length [cm] | 6,5 (5;11,5) | 7,3 (5;13) | n.s | 7 (4;14) | n.s |
| local recurrences [n] | 0 | 0 | 0 | 3 | 3 |
| metastases [n] | 0 | 0 | 0 | 2 | n.s |
| non union [n] | 2 (40%) | 2 (11,8%) | 0 | 1 (8,3%) | 0 |
| infection [n] | 0 | 0 | 1 minor postoperative (11%) | 0 | 0 |
| allograft fracture [n] | 0 | 2 (11,8%) | 1 (11%) | 0 | 6 (25%) |
| joint instability [n] | 0 | 4 (23,5%) | 0 | 7 (58,3%) | 0 |
| reoperations [n] | 2 | 3 | 4 | 3 | 14 |
| failed | 0 | 1 | 0 | 1 | 8 |
| survival | 100% at 3 years | 94,1% at 4,9 years | 100% at 3,5 years | 91,7% at 4,3 years | 66% at 10,9 years |
| flexion/extension [°] | 38/60 | 56/58 | 26/52 | 51/37 | 36/21 |
| pronation/supination [°] | 77/76,7 | 80/84 | 80/67 | n.s | 72/58 |

*Table 2.6: Literature review about osteoarticular allografts for distal radius part 1; range and percentage in round braces*

| | Asavamongkolkul A. et al. * | Vander Griend R.A. et al. * | Gitelis S. et al * | Cheng CY et al. * | Harness N.G. et al.* |
|---|---|---|---|---|---|
| journal&year | Int Orthop 2009 | JBJS Am 1993 | JBJS Am 1993 | CORR 2000 | J Hand Surg Am 2004 |
| patients [n] | 8 | 1 | 4 | 4 | 15 |
| dominant hand [n] | n.s | 1 | n.s | n.s | n.s |
| age [years] | 40,3 (21;61) | 22 | 33 (23;55) | 41,5 (27;72) | (31) |
| follow up [months] | 52, 7 (41,5;90,9) | 36 | 80,5 (43;105) | 60 (36;96) | 228 |
| resection length [cm] | 8,3 (6,5;12) | n.s | n.s | n.s | n.s |
| local recurrences [n] | 0 | 0 | 0 | 0 | 2 |
| metastases [n] | 1 | 0 | 0 | 0 | 0 |
| non union [n] | 2 (25%) | 0 | 0 | 0 | 2 (13,3%) |
| infection [n] | 0 | 0 | 0 | 0 | 0 |
| allograft fracture [n] | 1 (12,5%) | 1 | 0 | 0 | n.s |
| joint instability [n] | 0 | 1 | 1 (25%) | 4 (100%) | 2 (13,3%) |
| reoperations [n] | 3 | 2 | 0 | 0 | 15 |
| failed | 1 | 1 | 0 | 0 | 4 |
| survival | 87,5% at 4,4 years | | 100% at 6,7 years | 100% at 5 years | 73,3% at 19 years |
| flexion/extension [°] | 35/40 | n.s | n.s | 39/51 | n.s |
| pronation/supination [°] | 50/70 | n.s | n.s | n.s | n.s |

*Table 2.7: Literature review about osteoarticular allografts for distal radius part 1; range and percentage in round braces*

### 2.3.5 Osteoarticular allograft reconstructions around the knee

Results of literature review concerning osteoarticular allograft reconstructions of distal femur and proximal tibia are summarised in table 2.8 and table 2.9. One Argentinean group around Muscolo DL reported quite good results with 65% to 78% allograft survival at five and ten years. In one study including only patients with giant cell tumour close to the knee even 91% of all osteoarticular grafts survived at seven years on average. Other authors observed lower survival rates ranging between 36% and 78% after round about five years and between 43% and 68% at ten years.

The Argentinean group observed also low complication rates with reported incidence of fractures between 1.8% and 5.8% and infection occurring in 4.4% to 25%, but they did not specified their nonunion rates. In other reports complication rates are higher as incidence of fracture is recorded between 14.4% and 45.5% and that of infection varies from 5.2% to 25%. Nonunion was observed in 0 to 34%.

Joint degeneration in all forms from joint space narrowing to articular collapse, is a well-known complication in osteoarticular allografts and is recorded from 8.3% to 80.8% in reconstruction of distal femur or proximal tibia and with lengthened follow-up the incidence of joint degeneration increases. Total knee arthroplasty with preservation of allograft bone stock is reported in up to 34.6%.

Overall, the functional outcome reported in literature was satisfying. (13, 80, 82, 83, 91, 104, 117, 119, 139, 145, 156, 189)

| | Muscolo D.L. et al. | Muscolo D.L. et al. | Muscolo D.L. et al. | Muscolo D.L. et al.* |
|---|---|---|---|---|
| journal & year | CORR 2010 | JBJS Am 2005 | CORR 2000 | JBJS Br 1993 |
| patients [n] | 52 | 71 | 114 | 45 |
| age [years] | 24 (10;54) | 25 (8; 54) | 25 (8;68) | 28* |
| follow up [months] | 123 (10;250) | 82 (1;368) | 98 (36;360) | 84 (24;288)* |
| distal femur [n] | 0 | 71 | 73 ** | 25 |
| proximal tibia [n] | 52 | 0 | 45 ** | 20 |
| length of defect [cm] | n.s | 36%(10;80) of femur | n.s | n.s |
| CTX | 28 | 34 | n.s | 0 |
| local recurrence | 4 | 4 | 8 | 1 |
| DOD | 8 | 15 | 18 | 0 |
| allograft fracture [n] | 3 (5,8%) | 2 (2,8%) | 2 (1,8%) | 1 (2,2%) |
| Infection [n] | 13 (25%) | 5 (7%)** | 13 (11,4%) | 2 (4,4%) |
| non union [n] | n.s | n.s | n.s | 0 |
| failed [n] | 20 | 12** | 26 | n.s |
| years to graft removal | all were removed during first 4 years p.op | all were removed during the first 3 years p.op | 2,3 (1;5) | n.s |
| function [[1]MSTS; [2]Mankin score; [3]MSTS in %] | 26 (17;30)[1] | 26 (15;30)[1] | n.s | 33 good or excellent; 8 fair, 4 failure[2] |
| joint degeneration | 23 (44,2%) | 17 (35%) | 36% | n.s |
| articular resurfacing | 4 (7,8%) | 4 (9,9%)%) | 5 (4,4%) | 1 (2,2%) |
| allograft survival 5y/10y [%] | 65/65 | 78/78 | 73/-- | 91% at 7 years |
| limb perservation rate 5y/10y [%] | 91/91 | 97/97 | 93/-- | 100% at 7 years |
| amputations [n] | 5 | 2 | 7 | 0 |

*Table 2.8: Literature review about osteoarticular allografts about the knee part 1; range and percentage in round braces; *including patients with osteoarticular allograft in other locations, or patients with other type of reconstruction as intercalary allograft or allograft-prosthesis; ** including second osteoarticular allografts*

| | Toy P.C. et al. | Brigman B.E. et al.* | Rödl R.W. et al.* | Hornicek F.J. Jr. et al. | Clohisy D.R. and Mankin H.J. | Mnaymneh W. et al. | Zatsepin S.T. and Burdygin V.N. | Brien E.W. et al. * |
|---|---|---|---|---|---|---|---|---|
| journal & year | CORR 2010 | CORR 2004 | JBJS Br 2000 | CORR 1998 | JBJS Am 1994 | CORR 1994 | CORR 1994 | CORR 1994 |
| patients [n] | 26 | 72 | 11 | 38 | 16 | 96 | 156 | 8 |
| age [years] | 23 (10;58) | 14,4 * | 13,9 (11,1;19,2) | 36 (13;65) | 26 (17;46) | 28 (9;78) | n.s | 27,6 (14;49) |
| follow up [months] | 156 (15;283) | 66,4 * | 66 (61;74)* | 72(24;96) | 108 (72;168) | 52,8 (24;168) | ~20y | 34,8 (11;72) |
| distal femur [n] | 26 | 39 | 4 | 0 | 0 | 96 | 88 | 0 |
| proximal tibia [n] | 0 | 33 | 7 | 38 | 16 | 0 | 68 | 8 |
| length of defect [cm] | 19 (13,5;28) | distal femoral 21,3; proximal tibia 17,2 | 15,8 (11;28) | 12 (8;18) | 11,5 (7,5;23) | (8;28) | n.s | 12,8 (5,5;18) |
| CTX | 20 | 72 | 11 | 26 | n.s | 41 | n.s | 5 |
| local recurrence | 1 | n.s | 0 | 0 | 2 | 3 | 4 | 0 |
| DOD | 7 | n.s | 1 | 5 | 0 | 11 | 9 | 0 |
| allograft fracture [n] | 5 (19,2%) | 27% * | 5 (45,5%) | 14 (36,8%) | 5 (31,3%) | 14 (14,5%) | 35 (22,4%) | 2 (25%) |
| infection [n] | 6 (23,1%) | 16 % * | 1 (9%) | 7 (18,4%) | 2 (12,5%) | 5 (5,2%) | 16 (10,3%) | 2 (25%) |
| non union [n] | 5 (19,2%) | 34% * | 3 (17,6%)* | 4 (10,5%) | 2 (12,5%) | 15 (15,6%) | 0 | 0 |
| failed [n] | 10 | femoral 56%; tibial 24% | 7 | 15 | 7 | 14 | 30 | 3 |
| years to graft removal | 6,5 (1;17,7) | n.s | 2,3 (0,8;3,2) | n.s | 6 between 2 and 5 years p.op, 1 after 7 years | n.s | n.s | n.s |
| function [[1]MSTS; [2]Mankin score; [3]MSTS in %] | n.s | 33% excellent or good femoral; 61% excellent or good tibial[2] | 83,8% (76;90)[3] | 25 excellent or good; 6 fair, 7 poor[2] | 7 excellent or good; 9 fair or a failure[2] | 47 excellent or good; 22 fair, 14 poor[2] | 31% good or excellent; 45% fair, 24% poor or failure[2] | 10 excellent or good; 6 fair, 1 poor [1] |
| joint degeneration | 8 (30%) | 7 (9,7%) | n.s | n.s | 5 (31,3%) | 8 (8,3%) | 126 (80,8%) | 4 (50%) |
| articular resurfacing | 9 (34,6%) | 8 (11,1%) | n.s | 7 (18,4%) | 0 | 13 (13,5%) | 0 | 0 |
| allograft survival 5y/10y [%] | 69/63 | 78/68 tibial; 77/43 femoral | 36% at 5,5 years | 60,5% at 6 years | 56% at 9 years | 85,4% at 4,4 years | 80,8% at ~ 20 years | 62,5% at 2,9 years |
| limb perservation rate 5y/10y [%] | 96,2% at 13 years | 96/53 tibial; 94/84 femoral | 100% at 5,5 years | 92 % at 7 years | 87,5% at 9 years | 96,9% at 4,4 years | 93,6% at ~ 20 years | 75 % at 2,9 years |
| amputations [n] | 1 | 13 | 0 | 3 | 2 | 3 | 10 | 2 |

*Table 2.9: Literature review about osteoarticular allografts about the knee part 2; range and percentage in round braces; *including patients with osteoarticular allograft in other locations, or patients with other type of reconstruction as intercalary allograft or allograft-prosthesis*

### 2.3.6 Allograft prosthesis composite reconstruction of proximal femur

Again results of literature review regarding allograft prosthesis composite reconstructions of proximal femur are summarised and presented in table 2.10 and table 2.11. Reconstruction survival ranges between 76% and 100% at five years and between 76% and 81% at ten years.

| authors | Biau D.J. et al. | Biau D.J. et al. | Farid Y. et al. ** | Langlais F. et al. |
|---|---|---|---|---|
| journal & year | CORR 2010 | J Surg Oncol 2008 | CORR 2006 | CORR 2003 |
| patients [n] | 32 | 18 | 20 | 21 |
| age [years] | 41 (27;57) | 44 (18;76) | 44 (17;64) | 38 (14;77) |
| follow-up [months] | 68 (2;232) | 83 (25;232) | 76 (24;335) | 68,8 (3;180) |
| CTX/RTX [n] | 13/2 | 5/0 | n.s | 12/2 |
| allograft length [cm] | n.s | n.s | n.s | n.s |
| resection length [cm] | 175 (150;211) | n.s | 19,8 (13;25) | 18 (10;27) |
| local recurrens [n] | 4 | 0 | 0 | 6 |
| DOD [n] | 10 | 1 | 8 | 7 |
| nonunion [n] | 1 (3,1%) | 1 (5,6%) | 2 (10%) | 6 (28,6%) |
| fracture [n] | 0 | 0 | 0 | 0 |
| loosening [n] | 2 (6,3%) | 1 (5,6%) | 0 | 4 (19%) |
| infection [n] | 4 (12,5%) | 4 (22,2%) | 1 (5%) | 0 |
| dislocations [n] | n.s | 3 (16,7%) | 2 (10%) | 0 |
| failed [n] | 9 | 5 | 1 | 5 |
| Composite survival 5y/10 y [%] | 88/81 | 72,2% at 6,9 years | 100/85,7 | 90/81 |
| function [$^1$HHS; $^2$MSTS 1993 [%]; $^3$MSTS 1987] | n.s | 90 (48;95)$^1$ | 82$^2$ | 77 (43;97)$^2$ {11 patients} |

*Table 2.10: Literature review about allograft prosthesis composite reconstructions of proximal femur part 1; range and percentage in round braces; ** comparison with endoprostheses*

| authors | Donati D. et al. | Anract P. et al. ** | McGoveran B.M. et al. | Hejna M.J. et al.* | Zehr R. et al. ** |
|---|---|---|---|---|---|
| journal & year | CORR 2002 | RCO 2000 | CJS 1999 | Semin Surg Onc 1997 | CORR 1996 |
| patients [n] | 27 | 21 | 16 | 11 | 16 |
| age [years] | 32 (11;64) | 40 (15;67) | 51 (25;83) | 36 (12;71)* | 40,7 (13;66) |
| follow-up [months] | 58 (11;126) | 50 (6;120) | 47 (24;93) | 45,1 (11;124)* | n.s |
| CTX/RTX [n] | 8/0 | 10/5 | n.s. | 12/4* | 2/2 |
| allograft length [cm] | n.s | n.s | n.s. | 14,8 (10;20)* | 17 (7;29) |
| resection length [cm] | 14 (6;22) | 17,7 (5;30) | n.s. | n.s | n.s |
| local recurrens [n] | 0 | 0 | n.s. | 0 | 3 |
| DOD [n] | 5 | 5 | 5 | n.s | 3 |
| nonunion [n] | 4 (14,8%) | 0 | 3 (18,8%) | 5 (22,7%)* | 2 (12,5%) |
| fracture [n] | 4 (14,8%) | 0 | 3 (18,8%) | 0 | 0 |
| loosening [n] | 0 | 3 (14,3%) | 0 | 0 | 1 (6,3%) |
| infection [n] | 1 (3,7%) | 2 (9,5%) | 3 (18,8%) | 0 | 3 (18,6%) |
| dislocations [n] | n.s | 1 (4,8%) | 0 | 0 | 0 |
| failed [n] | 2 | 3 | 4 | 1 | 4 |
| Composite survival 5y/10 y [%] | 92,6% at 4,8 years | 77/77 | 75% at 3,9 years | 90,9% at 3,8 years | 76/76 |
| function [[1]HHS; [2]MSTS 1993 [%]; [3]MSTS 1987] | 92 (75;100)[2] | 83 (43;90)[2] | 58,3 (0;90)[2] | 28,3 (19;35)* [3] | 87 (67;97)[2] |

*Table 2.11: Literature review about allograft prosthesis composite reconstructions of proximal femur part 2; range and percentage in round braces; * also APC at other location; ** comparison with endoprostheses*

Common complications in this type of allograft reconstruction are nonunion occurring in up to 28.6% and infection with incidences up to 22.2%. Fracture is rare in composite allografts for proximal femur as only two authors observed fractures in 14.8% and 18.8% of reconstructions. A well-known complication in all prosthetic reconstructions is aseptic loosening which is reported in 0 to 16.7% of allograft prosthetic composite reconstructions of proximal femur. Dislocation – a common complication in reconstructions of proximal femur – was recorded between 0 and 16.7%.

Only McGoveran et al. reported a moderate functional outcome but apart from that the functional outcome is generally observed to be good. (107, 108, 115, 120, 121, 140, 152, 166, 173)

### 2.3.7 Allograft prosthesis composite reconstructions of proximal humerus

Findings of literature review regarding allograft prosthesis composite reconstructions of proximal humerus are summed up in table 2.12. Reported survival of allograft composite reconstructions for proximal humerus ranges between 83.3% and 100% around five years and only Abdeen et al. reported a ten year survival rate with 88%.

Nonunion rates are recorded between 0 and 50%, those of infection between 0 and 20%. Only two authors observed fractures, van de Sande et al. found 20% incidence of fracture and Potter et al. recorded 6.3% fractured grafts. Aseptic loosening was only reported by Abdeen et al. with 8.3% and by Kassab et al. who observed one aseptic loosening in seven allograft composite reconstructions with inverted prosthesis. Joint instability as subluxation and/or dislocation is reported in up to 40%.

Overall, satisfying functional results were found in literature. (63, 74, 141-144, 160)

| authors | Black A.W. et al. | van de Sande M.A.J. et al. | Dudkiewicz I. et al. | Potter B.K. et al. * | Jensen K.L. and Johnston J.O.** | Abdeen A. et al. | Kassab M. et al. *** |
|---|---|---|---|---|---|---|---|
| journal&year | J Shoulder Elbow Surg 2007 | Int Orthop 2010 | Cell Tissue Bank 2003 | CORR 2009 | CORR 1995 | JBJS Am 2009 | Rev Chir Orthop 2005 |
| patients [n] | 6 | 10 | 11 | 16 | 4 | 36 | 3 [7] |
| age [years] | 40,7 (15;73) | 34 | 31,3 (17;74) | 56,3 | 43 (23;74) | 23 (6;74) | 37,5 (13;76) ** |
| follow-up [months] | 55 (26;76) | 120 (9;300) | 67,6 (12;108) | 113 (24;214)* | 26,5 (24;31) | 60 (4;132) | 85 (16;300) ** |
| dominant arm [n] | 3 | n.s. | 5 | n.s | 11** | n.s | n.s |
| CTX/RTX [n] | 1/0 | n.s./0 | 10/0 | n.s/3 | n.s | 28/0 | 11/n.s ** |
| resection length [cm] | n.s | 12 (7;20) | 13 (7;21) | 12,5 | n.s | n.s | 13 (8;20) ** |
| local recurrence [n] | 0 | 0 | 0 | 1 | 0 | 1 | 7 ** |
| DOD [n] | 0 | 1 | 1 | 6 | 0 | 11 | 5 ** |
| nonunion [n] | 1 (16,7%) | 0 | 2 (18,2%) | 1 (6,3%) | 2 (50%) | 5 (13,9%) | 1 [0] |
| fractures [n] | 0 | 2 (20%) | n.s | 1 (6,3%) | 0 | 0 | 0 [0] |
| infections [n] | 0 | 2 (20%) | 2 (18,2%) | 2 (12,5%) | 0 | 1 (2,8%) | 0 [0] |
| subluxations [n] | n.s | 3 (30%) | n.s | 3 (18,8%) | 0 | n.s | 2 [0] |
| dislocations [n] | 0 | 1 (10%) | 1 (9,1%) | 0 | 0 | 1 (2,8%) | 1 [0] |
| aseptic loosening [n] | n.s | n.s. | n.s | 0 | 0 | 3 (8,3%) | 0 [1] |
| failed [n] | 1 | n.s. | 0 | 1 | 0 | n.s | n.s |
| survival rate 5y/10y [%] | 83,3% at 4,6 years | 90/-- | 100% at 5,6 years | 91/-- | 100% at 2,2 years | 88/88 | n.s |
| MSTS [%] | 69 | 72 | n.s | 79 | 4 Excellent | 26 (20;30) | 76 [88] |

*Table 2.12: Literature review about allograft prosthesis composite reconstructions of proximal femur; range and percentage in round braces; *comparison with osteoarticular allografts and/or prostheses; **also including patients reconstructed with other methods; ***results of composite allografts with inversed prosthesis in brackets*

## 2.4 Discussion

### 2.4.1 Intercalary reconstructions in lower limb

Indication for intercalary resection and reconstruction depends on tumour extent. Due to more accurate imagine techniques and improved multimodal treatment concepts intercalary resection without compromising safe wide resection margins is even possible if only little juxtaarticular bone is tumour free. In children and adolescent patients preservation of at least a part of epiphyseal segment affords further growth and provides or reduces limb length discrepancy. If tumour spread allows preservation of adjacent joint and intercalary resection the function is expected to be superior, since no joint replacement – neither prosthetic nor allograft – could function better than an intact native joint. (46, 150, 153, 164, 190)

Massive allografts are popular to reconstruct intercalary defects secondary to tumour resection. Intercalary allografts have a good reputation as they achieve best results compared with other allograft reconstructions, probably because reconstruction of joint and its associated complications as instability and joint degeneration are no issue. Allografts are easy to obtain – if there is access to a bone bank – in different sizes and lengths and their insertion and fixation is relatively easy. Massive allografts preserve bone stock, allow adequate attachment of salvaged tendons and provide initial mechanical strength. After healing, the graft may be progressively incorporated by host and it has been demonstrated that intercalary allografts can survive for decades. Ten year graft survival rates are reported about 80% ranging from 53% to 84% and if the allograft endures the first three years – thereafter infection and fracture are no longer issues – it achieves a steady state without detoriation of the graft suggesting that it will remain functional for the duration of patient's life. (14, 27, 28, 32, 33, 45, 46, 62, 78, 81, 93, 149, 153, 158, 163, 164, 172, 188, 189)

Good functional long-term results are achieved with intercalary allografts, but associated complications as nonunion, fracture and infection are frequent. Up to 70% require additional surgical interventions to get handle on complications and it has been proven that occurrence of one event of the triad infection, fracture and nonunion compromises final outcome. These main problems with allografts are – among other reasons – a consequence of the graft's avascular status and the incomplete revascularisation and incorporation by the host. (14, 33, 41, 45, 46, 62, 65, 66, 78, 81, 186)

To reduce these complications and improve the outcome the massive allograft can be combined with an autologous vascularised fibula. The allograft supplies initial mechanical strength and the fibula provides well-perfused bone and the capability of osteogenesis. (46, 181, 183, 185, 186) During the first years the allograft supports the narrow and weak fibula mechanically but it does not totally shield the fibula from weight bearing. This exposure to weight-bearing compression forces induces a progressive concentric fibular hypertrophy. Due to this hypertrophy the fibula can compensate weakening of the graft by the slow and incomplete process of creeping substitution what leads theoretically to a lower fracture risk. (46, 183, 187, 191) We observed four fractures in 14 patients (28.6%). One of them had an adequate trauma causing the fracture, he fell as one of his crutches had broken in the early mobilisation period when neither union nor hypertrophy of the fibula was completed. The other three fractures happened all subsequently to plate breakage and in femoral reconstructions. In literature no similar cases with plate breakage and consecutive fracture were found. The causation of plate breakage is unclear and should be an issue of interest for further biomechanical analysis. The well-perfused fibula is advantageous in treatment of fractures, since no graft had to be removed after fracture and all four fractured grafts healed similar to normal bone fractures after open reduction, replacement of internal fixation and autologous bone grafting. Similar observations concerning fracture healing in combined grafts – unless the anastomosis fails – are reported in literature. (30, 181-183, 185)

The osteogenic potential of the fibula improves not only fracture healing but allows also a more rapid and reliable fusion between both fibula and host as well as between allograft and host reducing the risk of nonunion. Although nonunion rates in combined allograft and vascularised fibula reconstructions are also reported up to 31%, overall reported nonunion rates seem to be indeed lower than in reconstructions with allografts alone. (27, 28, 49, 62, 149, 153, 155, 164, 172, 178-187, 192) Among the 14 patients operated at the Department of Orthopaedics Graz, three developed nonunion. One of them had more a delayed union, than a real nonunion, since the junction healed without further treatment after 18 months. The other two patients with nonunion were successfully treated with ESWT. Reports about treatment of nonunions in any type of allograft reconstructions with ESWT were not found in literature, but in these two patients it brought union, sparing them an additional surgical intervention.

The prolonged surgical time caused by harvesting of the fibula and the vascular anastomosis theoretically increases the risk of infection, but recorded infection rates are similar and on average even slightly lower than if allograft is used alone. Infection in combined allograft vascularised fibula reconstructions is a severe complication, but the fibula has the ability to survive infection. This may be, because antibiotics and host defences have better chances to get and work where they are needed by reason of its vascularity and are not walled of by the slow and incomplete revascularisation of allografts. (49, 62, 149, 153, 163, 164, 172, 178-183, 185, 187, 188) In our series of 14 patients two deep infections occurred (14.3%). Unfortunately one of them died of progressive tumour disease, before infection treatment could be started. In the other case the graft could be salvaged as infection was treated with systemic antibiotic therapy and removal of affected hardware.

As already mentioned the vascularised fibula expedites union and with faster achievement of stable graft-host union the time to full unrestricted weight bearing is reduced. We allowed partial weight bearing on average 2 months after reconstruction surgery and full weight bearing at 8.9 months postoperative, which is quite earlier than in other reported series. (155, 178, 180, 182-187, 192) To achieve early full function including unrestricted weight bearing is important for patients especially for young ones and we found no correlation of time to weight bearing and incidence of fracture or any other complication. Innocenti et al. (183) and Abed et al. (182) restricted weight bearing longest with 21.6 and 21.4 months to full weight bearing and observed fracture rates of 28.5% and 36% anyway.

Presence of the vascularised fibula improves the revascularisation and subsequent bone remodelling of the allograft, which favours early fusion between fibula and allograft, forming a single durable diaphysis. This appearance of new remodelling under weight bearing mechanical forces is an indicator for the viability of the reconstruction. (48, 187, 191)

If the fibula is implanted with an intact growth plate in children, potential growth may be obtained. (30, 187) By the time of writing, limb length discrepancy is no issue in our series, but the young patients, where this could be a problem, are not full-grown to date.

The combination of an allograft with an autologous vascularised fibula has also disadvantages, such as the prolonged surgery time, the need of microsurgical skills for vascular anastomosis and the risk of anastomosis' failure by thrombosis. It is also important to keep donor side morbidity following harvest of the fibula in mind. A flexion deformity of the big toe is the most common observed donor side complication. We found this complication in three patients not really compromising them. Other donor side complications recorded in literature are pain, peroneal nerve palsy, wound healing disorder and ankle joint instability. (179, 182, 183, 185, 187)

Complications are quite frequent in this reconstruction type as 43% of our patients needed at least one additional surgical intervention to treat complications and similar rates are reported in literature. But despite this frequency complications are manageable and only few grafts fail. In our series we found a five year survival rate of 100% and in literature midterm survival rates are also reported ranging between 80% and 100%. (177-182, 184-186) Capanna et al. (187) reported the series with longest follow up and found 93.3% graft survival after 9 years of follow up on average, what compares favourable to single allograft reconstructions. Although long term survival is rarely reported, (183, 187) it can be suggested that - similar to single allograft reconstructions – survival rates will not further decline and the construct becomes a stable and durable system.

Intercalary endoprostheses are a less popular alternative to allograft reconstructions. Only a few articles dealing with this subject are published and caution is advised in comparison of the results with intercalary allograft reconstructions, as patients are older in endoprosthetic series and treatment of metastatic disease is also included as indication. Endoprosthetic reconstruction offers ease of application, early weight bearing and normal function and complications with union cease to exist. Infection and prosthetic or periprosthetic fracture are also issues in prostheses and additionally they have complications as aseptic loosening and mechanical wear. (46, 131, 132, 134) Infection and fracture rates are relatively low ranging from 0 to 3.6% and from 0 to 16% but aseptic loosening is the major problem occurring in up to 33%. (131-135)

The major concern with the use of endoprostheses in young patients is their high potential for late failure. While allografts achieve a stable state after the first years, endoprostheses continues to fail. (27, 45, 81, 93, 131, 132, 135) Hanna et al. (131) recorded a five year survival rate of 85% that declined to 68% at 10 years and Aldlyami et al. (134) published the series with the longest follow up and reported a ten year survival rate of 63% and the curve is still declining, without achieving a stable plateau. The latter authors even wrote, that they do not recommend intercalary endoprostheses in tibial reconstructions except in a palliative situation, but called it an attractive option in femoral defects. But as endoprostheses seem to be inferior to allografts in their durability, they should be used where immediate weight bearing and full function is of greater concern than durability, like in patients with metastatic disease.

### 2.4.2 Osteoarticular allografts for distal radius reconstructions

Reconstruction of a skeletal defect of the distal part of the radius following tumour resection is challenging. Skeletal reconstruction as well as functional restoration is required because of the high functional demands of the hand. Challenging factors in attempt to reconstruct a stable and functional wrist are limited surrounding soft tissues, the proximity of adjacent nerves and tendons and the relatively avascular host bed as the main components of the wrist are bones and tendons and muscles – preserving much of the blood supply – are limited. (116, 168, 193-196)

In patients – like manual workers – who need a strong and stable wrist that can withstand high loads, arthrodesis is the method of choice. Arthrodesis provides stability at the cost of wrist motion, what may cause some impairment in daily live activities. Despite this loss of wrist motion, good results are generally reported with satisfying function of wrist in daily live activities with little to no restrains. Autologous fibula, vascularised or nonvascularised, is the preferred graft for arthrodesis, but tibial cortex, iliac crest and ulna are also possible bone grafts. Nonvascularised fibula grafts are easier to harvest and implant but the graft is only slowly incorporated. Union time is significantly extended in nonvascularised bone grafts and nonunion is a frequent complication. Although earlier union can be expected with the use of a vascularised fibular graft, nonunion cannot be avoided totally. The use of a vascularised fibula is technically demanding and entails prolonged operation time. (75, 77, 127, 168, 193, 196-198)

To preserve some wrist motion a partial arthrodesis can be done with fixing the graft only to the scapholunate portion of the carpal row. Partial arthrodesis can provide a stable and pain free wrist with sufficient range of motion for daily live activities. (75, 197, 199) Some good results were reported with this method (197, 199) and Muramatsu et al. (197) recommend partial arthrodesis especially for young patients with high activity in daily living.

In attempt to preserve full wrist function the proximal fibula – again nonvascularised or vascularised – is commonly used for arthroplasty because of its similarity in shape and size to distal radius. In children a vascularised fibula additionally provides the possibility of epiphyseal transfer and thereby further longitudinal growth and avoidance of developing a radial club hand. Fibula arthroplasty achieves good to excellent functional results with satisfying range of motion, but instability and degenerative change of carpofibular joint are frequently observed. Despite these complications, in most cases only minimum pain and little limitation in daily living is observed. The low level of pain is suspected to be a result of denervation of wrist joint during surgery. Articular degeneration was thought to be a result of the lack of viability in nonvascularised fibula grafts, but although a vascularised fibula provides viable articular cartilage it cannot prevent joint degeneration due to the relatively incongruence of fibulocarpal articular surfaces. (76, 168, 193, 197-201)

Osteoarticular allografts offer best anatomical match with first carpal row, avoid donor side morbidity and operation time is shorter in comparison with autografts. Good to excellent functional outcome is reported but complications are also commonly recorded. In contrast to allograft reconstructions at other locations infection is rare in osteoarticular reconstructions of distal radius, (75-77, 116, 124-127, 168) only Szabo et al. (76) observed one minor infection. Nonunion and fracture are common complications with reported incidences up to 25% for both. (75-77, 116, 126, 168) No patient in our series sustained a fracture. All grafts were fixed with a long bridging plate, which seems to prevent fracture. (125) Two of our five patients (40%) developed nonunion but could be successfully treated with additional autologous bone grafting. The relatively avascular host bed at the wrist probably favours nonunion. Joint instability and articular degeneration are the complications most frequently observed in arthroplasties with osteoarticular allografts. (75-77, 116, 124-127, 168) None of the five patients in our series developed any form of instability but recorded incidences in literature are quit high. Cheng et al. (125) even found in all four patients some translocation of the graft. In most cases only mild instability occurs without disabling patients in their working or daily live activities and failure because of instability is rare, but instability accelerates degeneration of articular surface. Szabo et al. (76) additionally performed the Sauve-Kapandji procedure in their osteoarticular allograft reconstructions to prevent instability and found no form of joint instability at a medium follow up of 8.3 years. Degenerative changes of articular cartilage are observed in nearly all cases, but most patients reported no to only mild pain or disability in daily live activities and only few had to be revised due to arthritic disorders. (75-77, 116, 124-127, 168) We found degenerative changes in four of five patients but all were asymptomatic. The long term outcome and survival rates of osteoarticular allografts for distal radius are unclear. Kocher et al. (116) reported the study about osteoarticular allograft reconstructions of distal radius with the longest follow up of 10.9 years on average and 33% of the reconstructions failed. Seven patients received an arthrodesis as revision procedure and one patient had an amputation at an average of 8.1 years. Compared to intercalary reconstructions where most graft failures are happening in the first 3 years, osteoarticular reconstructions of the distal radius are failing later. Taking this into consideration it is quite possible that complications and failures will occur later in our study as well as in other studies with short follow-up.

Reconstruction of the distal part of radius with prostheses as a contingent alternative to bone grafts is scarcely reported and the early attempts with them were not encouraging. (202, 203) Hatano et al. (194) reported about two reconstructions with ceramic prosthesis over ten years. Both developed radial deviation and radiolucent lines but had no clinical symptoms and achieved acceptable range of motion and function of wrist and hand. Because of radial deviation and slight instability, the author would not recommend prosthetic reconstruction in cases with more extensive soft-tissue involvement to prevent subluxation and dislocation. Natarajan et al. (196) used a new designed bipolar hinge custom prosthesis in 24 patients and achieved satisfactory functional outcome and a ten-year prosthetic survival of 87.5%. Further investigations are necessary to obtain more information for considering a prosthetic reconstruction as acceptable alternative to bone grafts.

### 2.4.3 Osteoarticular allografts around the knee

If tumour extension requires an intraarticular resection to obtain safe margins around the knee reconstruction can be done with osteoarticular allografts, endoprostheses or a combination of these two, an APC.

Osteoarticular allografts are a biologic solution with biologic bone union and theoretically full incorporation by host by the process of creeping substitution. Allografts restore bone stock and contain a location for reattachment of host ligaments and tendons useful in attempts to restore joint stabilisation and motor function, especially the extensor mechanism in reconstructions of proximal tibia. With this method only the involved portion of joint is replaced and the opposite articular surface as well as the opposite growth plate are left intact. The allograft can be sized in length to the defect following resection and no additional resection of normal bone due to size – as in prosthesis – is required. (30, 31, 80, 82, 83, 91, 104, 117, 119, 139, 156, 189)

But osteoarticular allografts also have some disadvantages as the ligamentous reconstruction is technically demanding, rehabilitation period and the time to unrestricted weight bearing is prolonged. The greatest drawback in osteoarticular allograft reconstructions is their considerable high complication rate. Complications as infection, fracture and nonunion are frequent, they adversely affect the outcome and often lead to failure of reconstruction. Joint instability and degenerative joint disease are also common complications in osteoarticular allografts. (13, 14, 30, 80, 81, 83, 84, 91, 93, 117, 119, 139, 145, 156) In the series with longest follow up 70% received at least one additional operation and as most patients received one or more major complications affecting the outcome, excellent long term outcomes were rare. (84)

Instability is mostly caused by less than optimal reconstruction and anatomic incongruity of the allograft. If knee instability is neglected it accelerates degenerative arthritis. (78, 80) Despite cryoprotective agents it is not possible to maintain viability of cartilage and it is clear that cartilage on osteoarticular allografts degenerates with time, leading to degenerative joint disease. Degenerative arthritis occurs around five years after initial reconstructions and about 20% of patients need a total joint arthroplasty, whereby the allograft bone stock is mostly preserved. Late failures in osteoarticular reconstructions are mainly related to progressive joint detoriation and in a report about osteoarticular allografts with a mean follow up of 16 years Ogilvie et al. (84) work out that degenerative joint disease is a major event that can affect long term function and survival.

Because of the frequency of complications which often lead to failure of reconstruction the mid and long term graft survival rates are not encouraging with 10-year survival rates between 43% and 68%. (13, 80, 83, 91, 104, 117, 119, 145) The impressive results reported by the group around Muscolo are the exception with obvious lower complication rates and thereby improved survival rates. This is probably the result of their long experience and dedication to allograft surgery, an extensive bone bank and matching of allografts to patients using CT measurements. (80, 82, 139, 156, 189)

Muscolo et al. still recommend osteoarticular allograft reconstructions about the knee, while their use is discouraged by other authors. (30, 82-84, 119, 156) Toy et al. (83) wrote that, because of the frequency of these complications, their institution had not used osteoarticular reconstruction of distal femur in the past eight years and Donati et al. (30) suggested that because of the high incidence of subchondral fractures allograft prosthesis composite or endoprostheses are preferable.

Endoprosthetic reconstruction is technically easier than osteoarticular allograft reconstruction. Immediate stability and rapid return to full weight bearing is provided by endoprostheses. They have no biologic location for soft tissue reattachment but due to their non biologic constitution there are also no adverse effects from adjuvant therapy like chemotherapy or radiation. For endoprosthetic reconstruction the whole joint must be resected and both growth plates are sacrificed, probably leading to relevant limb length discrepancy. With the use of an endoprostheses allograft specific complications as nonunion and degenerative joint disease are avoided, but they share some complications with allografts as infection and fracture – prosthetic and periprosthetic – and additionally have their own problems predominantly aseptic loosening. The main concern in the use of prostheses – especially in young patients – is late failure. But in recent reports overall complication rates are lower than in osteoarticular allografts. Recorded survival rates are encouraging, reaching or even exceeding those reported by Muscolo et al. with allografts. (204-209)

Allograft prosthesis composite reconstructions share the benefits of both allografts and endoprostheses. It combines the mechanical stability of prosthesis with the biologic reconstruction of extensor mechanism due to soft tissue reattachment to the allograft. Infection rates are higher in composite reconstructions than in endoprostheses, but aseptic loosening is less frequent and final outcome and survival rates are similar in both reconstruction types. (107, 167, 169, 210, 211)

### 2.4.4 Allograft prosthesis composite reconstruction of proximal femur and proximal humerus

Reconstruction of proximal femur and proximal humerus are discussed together because there are some similarities. Endoprostheses and allograft prosthesis composite are the main reconstruction options for both wheras osteoarticular allograft reconstruction is not a suitable alternative because of the reported high complication and failure rates. (74, 78, 142, 148, 212)

Composite allografts offer the advantage of biologic and effective reattachment of tendons either of the hip abductors and iliopsoas muscle or of the rotator cuff. Soft tissue reconstruction is suggested to improve stability and function. Composite reconstructions restore bone stock, provide an improved anchorage into the host bone and avoid stress shielding by transmission of loading forces by the graft to the host bone. Reconstruction with allograft prosthesis composite is a more complex and technically demanding surgical procedure. The allograft makes the construct susceptible for allograft related complications as infection, fracture and nonunion and entails a prolonged rehabilitation period. (74, 78, 107, 108, 115, 120, 121, 140, 142-144, 152, 160, 166)

Implantation of endoprostheses is quicker and easier and provides early return to full function. Endoprostheses avoid the risk of allograft related complications as nonunion and the potential risk of disease transmission. But instability – probably as a consequence of the lack of an effective anchor for soft tissue reattachment – is a frequent complication with endoprostheses at both locations the proximal femur and the proximal humerus. Another problem with endoprostheses is mechanical wear and aseptic loosening with its possible influence on longevity of the reconstruction. (74, 108, 120, 121, 141, 142) Compared with other anatomic regions, however, the proximal humerus has had favourable implant longevity after endoprosthetic reconstruction. (74, 110, 129, 142, 209)

Infection rates are reported to be higher in allograft prosthesis composites than in endoprosthetic reconstructions, which is probably attributable to greater complexity and longer operation time of this reconstruction method. With recorded incidences ranging between no infection and up to 28% of reconstructions, infection rates are similar to those of massive allograft reconstructions in general. (33, 63, 74, 83, 92, 93, 107, 108, 115, 117, 118, 120-122, 140-145, 152, 156, 160, 166, 173)

Fractures are observed less frequent in composite allografts than in other allograft reconstructions. Intramedullary fixation with a long stem prosthesis bypassing the graft host junction seems to prevent the allograft from fracture. (33, 63, 70, 74, 81, 93, 107, 108, 115, 120, 121, 140-145, 150-152, 154, 157, 160, 166, 173)

Functional results were found to be slightly better in composite reconstructions compared with endoprostheses in humeral as well as in femoral reconstructions. This is likely the result of improved soft tissue reconstruction by biologic reattachment of tendons to the allograft. The effective fixation of muscles to the graft improves also stability as there is a tendency to reduced subluxation and dislocation rates especially in proximal femur reconstructions. (74, 108, 115, 120, 121, 141, 142, 166)

Survival rates of endoprosthetic and composite reconstructions were encouraging and similar in both groups. At proximal femur allograft prosthesis composite reconstructions have a higher rate of early failure but reach a stable state after three to five years while endoprosthetic reconstructions are not reaching such a plateau. In humeral reconstructions survival is reported to be slightly better in endoprosthetic reconstructions than in composite allografts. (74, 78, 108, 120, 121, 142, 166)

There is a general agreement that allograft prosthesis composite reconstructions are a stable and durable reconstructive option with acceptable complication rates and good functional results in reconstruction of proximal femur and proximal humerus. Composite reconstructions are recommended by the majority of authors for young and active patients with primary malignancy. (63, 107, 120, 121, 142, 166, 167, 174,160)

## 2.5 Conclusion

Recapitulatory, massive bone allografts provide a durable reconstructive solution for skeletal defects after tumour resection that can function well for the whole duration of patients' life, but not all variations of allograft reconstructions have this durability.

Reconstruction with an intercalary allograft combined with an autologous vascularised fibula seems to be the best way to use allografts. Graft survival rates are high despite the frequency of complications as most of them can be successfully treated without compromising the final outcome.

The combination of a massive allograft with a standard prosthesis is an attractive option if tumour spread requires resection and following reconstruction. Allograft prosthesis composite reconstructions are advantageous in restoration of a functional and stable joint and their durability is equal to those of endoprosthetic reconstructions.

For most authors, however, osteoarticular allografts are not the method of choice for reconstruction of skeletal defects involving the joint, because of the high complication and failure rates. The reconstruction of distal radius is an exception. Although there are also some problems with joint degeneration and instability, it appears that osteoarticular allografts are the best solution to reconstruct skeletal defects at this location in terms of function, durability and avoidance of donor side morbidity.

Allografts are a great option in limb salvage surgery, but their usage must be considered together with other reconstructive alternatives in regard of tumour's localisation and characteristics as well as of patient's needs and expectations.

# 3 References

(1) Macewen W. I. The Os teogenic Factors in the Development and Repair of Bone. Ann Surg 1887 Oct;6(4):289-306.

(2) Macewen W. I. Intrahuman Bone Grafting and Reimplantation of Bone. Ann Surg 1909 Dec;50(6):959-968.

(3) Lexer E. The use of free osteoplasty together with trials on arthrodesis and joint transplantation. Archiv fur klin Chirurgie. 1908;86(4):939-954. Clin Orthop Relat Res 2008 Aug;466(8):1771-1776.

(4) Perry CR. Bone repair techniques, bone graft, and bone graft substitutes. Clin Orthop Relat Res 1999 Mar; (360):71-86.

(5) Tomford WW. Bone allografts: past, present and future. Cell Tissue Bank 2000;1(2):105-109.

(6) Herndon CH, Chase SW. Experimental studies in the transplantation of whole joints. J Bone Joint Surg Am 1952 Jul;24-A(3):564-578.

(7) Chase SW, Herndon CH. The fate of autogenous and homogenous bone grafts. J Bone Joint Surg Am 1955 Jul;37-A(4):809-841.

(8) Curtiss PH,Jr, Powell AE, Herndon CH. Immunological factors in homogenous-bone transplantation. II. The inability of homogenous rabbit bone to induce circulating antibodies in rabbits. J Bone Joint Surg Am 1959 Dec;41-A:1482-1488.

(9) Curtiss PH,Jr, Chase SW, Herndon CH. Immunological factors in homogenous-bone transplantation. II. Histological studies. J Bone Joint Surg Am 1956 Apr;38-A(2):324-328; passim.

(10) Ottolenghi CE. Massive osteoarticular bone grafts. Transplant of the whole femur. J Bone Joint Surg Br 1966 Nov;48(4):646-659.

(11) Volkov M. Allotransplantation of joints. J Bone Joint Surg Br 1970 Feb;52(1):49-53.

(12) Parrish FF. Allograft replacement of all or part of the end of a long bone following excision of a tumor. J Bone Joint Surg Am 1973 Jan;55(1):1-22.

(13) Zatsepin ST, Burdygin VN. Replacement of the distal femur and proximal tibia with frozen allografts. Clin Orthop Relat Res 1994 Jun; (303):95-102.

(14) Mankin HJ, Springfield DS, Gebhardt MC, Tomford WW. Current status of allografting for bone tumors. Orthopedics 1992 Oct;15(10):1147-1154.

(15) Eilber F, Giuliano A, Eckardt J, Patterson K, Moseley S, Goodnight J. Adjuvant chemotherapy for osteosarcoma: a randomized prospective trial. J Clin Oncol 1987 Jan;5(1):21-26.

(16) Goorin AM, Abelson HT, Frei E,3rd. Osteosarcoma: fifteen years later. N Engl J Med 1985 Dec 26;313(26):1637-1643.

(17) Goorin AM, Frei E,3rd, Abelson HT. Adjuvant chemotherapy for osteosarcoma: a decade of experience. Surg Clin North Am 1981 Dec;61(6):1379-1389.

(18) Oberlin O, Patte C, Demeocq F, Lacombe MJ, Brunat-Mentigny M, Demaille MC, et al. The response to initial chemotherapy as a prognostic factor in localized Ewing's sarcoma. Eur J Cancer Clin Oncol 1985 Apr;21(4):463-467.

(19) Winkler K, Beron G, Delling G, Heise U, Kabisch H, Purfurst C, et al. Neoadjuvant chemotherapy of osteosarcoma: results of a randomized cooperative trial (COSS-82) with salvage chemotherapy based on histological tumor response. J Clin Oncol 1988 Feb;6(2):329-337.

(20) Winkler K, Bieling P, Bielack S, Delling G, Dose C, Jurgens H, et al. Local control and survival from the Cooperative Osteosarcoma Study Group studies of the German Society of Pediatric Oncology and the Vienna Bone Tumor Registry. Clin Orthop Relat Res 1991 Sep; (270):79-86.

(21) Bacci G, Picci P, Ferrari S, Ruggieri P, Casadei R, Tienghi A, et al. Primary chemotherapy and delayed surgery for nonmetastatic osteosarcoma of the extremities. Results in 164 patients preoperatively treated with high doses of methotrexate followed by cisplatin and doxorubicin. Cancer 1993 Dec 1;72(11):3227-3238.

(22) Rosen G, Caparros B, Huvos AG, Kosloff C, Nirenberg A, Cacavio A, et al. Preoperative chemotherapy for osteogenic sarcoma: selection of postoperative adjuvant chemotherapy based on the response of the primary tumor to preoperative chemotherapy. Cancer 1982 Mar 15;49(6):1221-1230.

(23) Rosen G, Marcove RC, Caparros B, Nirenberg A, Kosloff C, Huvos AG. Primary osteogenic sarcoma: the rationale for preoperative chemotherapy and delayed surgery. Cancer 1979 Jun;43(6):2163-2177.

(24) Simon MA, Aschliman MA, Thomas N, Mankin HJ. Limb-salvage treatment versus amputation for osteosarcoma of the distal end of the femur. 1986. J Bone Joint Surg Am 2005 Dec;87(12):2822.

(25) Grimer RJ, Carter SR, Pynsent PB. The cost-effectiveness of limb salvage for bone tumours. J Bone Joint Surg Br 1997 Jul;79(4):558-561.

(26) Simon MA, Aschliman MA, Thomas N, Mankin HJ. Limb-salvage treatment versus amputation for osteosarcoma of the distal end of the femur. J Bone Joint Surg Am 1986 Dec;68(9):1331-1337.

(27) Alman BA, De Bari A, Krajbich JI. Massive allografts in the treatment of osteosarcoma and Ewing sarcoma in children and adolescents. J Bone Joint Surg Am 1995 Jan;77(1):54-64.

(28) Cara JA, Lacleriga A, Canadell J. Intercalary bone allografts. 23 tumor cases followed for 3 years. Acta Orthop Scand 1994 Feb;65(1):42-46.

(29) Donati D, Capanna R, Campanacci D, Del Ben M, Ercolani C, Masetti C, et al. The use of massive bone allografts for intercalary reconstruction and arthrodeses after tumor resection. A multicentric European study. Chir Organi Mov 1993 Apr-Jun;78(2):81-94.

(30) Donati D, Di Liddo M, Zavatta M, Manfrini M, Bacci G, Picci P, et al. Massive bone allograft reconstruction in high-grade osteosarcoma. Clin Orthop Relat Res 2000 Aug; (377):186-194.

(31) Kohler R, Lorge F, Brunat-Mentigny M, Noyer D, Patricot L. Massive bone allografts in children. Int Orthop 1990;14(3):249-253.

(32) Muscolo DL, Petracchi LJ, Ayerza MA, Calabrese ME. Massive femoral allografts followed for 22 to 36 years. Report of six cases. J Bone Joint Surg Br 1992 Nov;74(6):887-892.

(33) Ortiz-Cruz E, Gebhardt MC, Jennings LC, Springfield DS, Mankin HJ. The results of transplantation of intercalary allografts after resection of tumors. A long-term follow-up study. J Bone Joint Surg Am 1997 Jan;79(1):97-106.

(34) Pape HC, Evans A, Kobbe P. Autologous bone graft: properties and techniques. J Orthop Trauma 2010 Mar;24 Suppl 1: 36-40.

(35) Khan SN, Cammisa FP,Jr, Sandhu HS, Diwan AD, Girardi FP, Lane JM. The biology of bone grafting. J Am Acad Orthop Surg 2005 Jan-Feb;13(1):77-86.

(36) Delloye C, Cornu O, Druez V, Barbier O. Bone allografts: What they can offer and what they cannot. J Bone Joint Surg Br 2007 May;89(5):574-579.

(37) Kruyt MC, Dhert WJ, Oner C, van Blitterswijk CA, Verbout AJ, de Bruijn JD. Osteogenicity of autologous bone transplants in the goat. Transplantation 2004 Feb 27;77(4):504-509.

(38) Cheng EY, Gebhardt MC. Allograft reconstructions of the shoulder after bone tumor resections. Orthop Clin North Am 1991 Jan;22(1):37-48.

(39) Pollock R, Stalley P, Lee K, Pennington D. Free vascularized fibula grafts in limb-salvage surgery. J Reconstr Microsurg 2005 Feb;21(2):79-84.

(40) Lyons AJ, James R, Collyer J. Free vascularised iliac crest graft: an audit of 26 consecutive cases. Br J Oral Maxillofac Surg 2005 Jun;43(3):210-214.

(41) Wang JW, Shih CH. Allograft transplantation in aggressive or malignant bone tumors. Clin Orthop Relat Res 1993 Dec; (297):203-209.

(42) Urken ML, Buchbinder D, Costantino PD, Sinha U, Okay D, Lawson W, et al. Oromandibular reconstruction using microvascular composite flaps: report of 210 cases. Arch Otolaryngol Head Neck Surg 1998 Jan;124(1):46-55.

(43) Sen MK, Miclau T. Autologous iliac crest bone graft: should it still be the gold standard for treating nonunions? Injury 2007 Mar;38 Suppl 1: 75-80.

(44) Morrison JG, Reilly DT. Allograft in Revision Total Knee Arthroplasty. In: Bono JV, Scott RD, editors. Revision Total Knee Arthroplasty. 1st ed. New York: Springer; 2005. p. 81-96.

(45) Hornicek FJ, Gebhardt MC, Sorger JI, Mankin HJ. Tumor reconstruction. Orthop Clin North Am 1999 Oct;30(4):673-684.

(46) Fuchs B, Ossendorf C, Leerapun T, Sim FH. Intercalary segmental reconstruction after bone tumor resection. Eur J Surg Oncol 2008 Dec;34(12):1271-1276.

(47) Nishida J, Shimamura T. Methods of reconstruction for bone defect after tumor excision: a review of alternatives. Med Sci Monit 2008 Aug;14(8):RA107-113.

(48) Ceruso M, Falcone C, Innocenti M, Delcroix L, Capanna R, Manfrini M. Skeletal reconstruction with a free vascularized fibula graft associated to bone allograft after resection of malignant bone tumor of limbs. Handchir Mikrochir Plast Chir 2001 Jul;33(4):277-282.

(49) El-Gammal TA, El-Sayed A, Kotb MM. Microsurgical reconstruction of lower limb bone defects following tumor resection using vascularized fibula osteoseptocutaneous flap. Microsurgery 2002;22(5):193-198.

(50) Amr SM, El-Mofty AO, Amin SN, Morsy AM, El-Malt OM, Abdel-Aal HA. Reconstruction after resection of tumors around the knee: role of the free vascularized fibular graft. Microsurgery 2000;20(5):233-251.

(51) Gebhardt MC, Roth YF, Mankin HJ. Osteoarticular allografts for reconstruction in the proximal part of the humerus after excision of a musculoskeletal tumor. J Bone Joint Surg Am 1990 Mar;72(3):334-345.

(52) Sarukawa S, Noguchi T, Oh-Iwa I, Sunaga A, Uda H, Kusama M, et al. Bare bone graft with vascularised iliac crest for mandibular reconstruction. J Craniomaxillofac Surg 2011 Feb; 24.

(53) Ting JW, Rozen WM, Leong J, Crock J. Free deep circumflex iliac artery vascularised bone flap for reconstruction of the distal radius: planning with CT angiography. Microsurgery 2010;30(2):163-167.

(54) Yücetürk A, Tuncay C, Isiklar U, Tandogan R. Vascularised bone graft applications in upper extremity problems. Microsurgery 1998;18(3):160-162.

(55) Hsu RW, Wood MB, Sim FH, Chao EY. Free vascularised fibular grafting for reconstruction after tumour resection. J Bone Joint Surg Br 1997 Jan;79(1):36-42.

(56) Zaretski A, Amir A, Meller I, Leshem D, Kollender Y, Barnea Y, et al. Free fibula long bone reconstruction in orthopedic oncology: a surgical algorithm for reconstructive options. Plast Reconstr Surg 2004 Jun;113(7):1989-2000.

(57) Friedrich JB, Moran SL, Bishop AT, Wood CM, Shin AY. Free vascularized fibular graft salvage of complications of long-bone allograft after tumor reconstruction. J Bone Joint Surg Am 2008 Jan;90(1):93-100.

(58) Friedrich JB, Moran SL, Bishop AT, Shin AY. Free vascularized fibula grafts for salvage of failed oncologic long bone reconstruction and pathologic fractures. Microsurgery 2009;29(5):385-392.

(59) Manabe J, Ahmed AR, Kawaguchi N, Matsumoto S, Kuroda H. Pasteurized autologous bone graft in surgery for bone and soft tissue sarcoma. Clin Orthop Relat Res 2004 Feb; (419):258-266.

(60) Poffyn B, Sys G, Mulliez A, Van Maele G, Van Hoorebeke L, Forsyth R, et al. Extracorporeally irradiated autografts for the treatment of bone tumours: tips and tricks. Int Orthop 2011 Jun;35(6):889-895.

(61) Poffyn B, Sys G, Van Maele G, Van Hoorebeke L, Forsyth R, Verstraete K, et al. Radiographic analysis of extracorporeally irradiated autografts. Skeletal Radiol 2010 Oct;39(10):999-1008.

(62) Chen TH, Chen WM, Huang CK. Reconstruction after intercalary resection of malignant bone tumours: comparison between segmental allograft and extracorporeally-irradiated autograft. J Bone Joint Surg Br 2005 May;87(5):704-709.

(63) Jensen KL, Johnston JO. Proximal humeral reconstruction after excision of a primary sarcoma. Clin Orthop Relat Res 1995 Feb;(311)(311):164-175.

(64) Voggenreiter G, Ascherl R, Blumel G, Schmit-Neuerburg KP. Extracorporeal irradiation and incorporation of bone grafts. Autogeneic cortical grafts studied in rats. Acta Orthop Scand 1996 Dec;67(6):583-588.

(65) Enneking WF, Campanacci DA. Retrieved human allografts : a clinicopathological study. J Bone Joint Surg Am 2001 Jul;83-A(7):971-986.

(66) Enneking WF, Mindell ER. Observations on massive retrieved human allografts. J Bone Joint Surg Am 1991 Sep;73(8):1123-1142.

(67) Stevenson S, Emery SE, Goldberg VM. Factors affecting bone graft incorporation. Clin Orthop Relat Res 1996 Mar; (324):66-74.

(68) Delloye C, Simon P, Nyssen-Behets C, Banse X, Bresler F, Schmitt D. Perforations of cortical bone allografts improve their incorporation. Clin Orthop Relat Res 2002 Mar; (396):240-247.

(69) Sigholm G, Gendler E, McKellop H, Marshall GJ, Moore TM, Sarmiento A. Graft perforations favor osteoinduction. Studies of rabbit cortical grafts sterilized with ethylene oxide. Acta Orthop Scand 1992 Apr;63(2):177-182.

(70) Thompson RC,Jr, Pickvance EA, Garry D. Fractures in large-segment allografts. J Bone Joint Surg Am 1993 Nov;75(11):1663-1673.

(71) Sorger JI, Hornicek FJ, Zavatta M, Menzner JP, Gebhardt MC, Tomford WW, et al. Allograft fractures revisited. Clin Orthop Relat Res 2001 Jan; (382):66-74.

(72) Ginat DT, Kenan S, Steiner GC. Osteoarticular allograft of the proximal humerus--histopathological study 18 years after implantation. Acta Orthop 2005 Dec;76(6):934-938.

(73) Matejovsky Z,Jr, Matejovsky Z, Kofranek I. Massive allografts in tumour surgery. Int Orthop 2006 Dec;30(6):478-483.

(74) van de Sande MA, Dijkstra PD, Taminiau AH. Proximal humerus reconstruction after tumour resection: biological versus endoprosthetic reconstruction. Int Orthop 2010 Nov 18.

(75) Scoccianti G, Campanacci DA, Beltrami G, Caldora P, Capanna R. The use of osteo-articular allografts for reconstruction after resection of the distal radius for tumour. J Bone Joint Surg Br 2010 Dec;92(12):1690-1694.

(76) Szabo RM, Anderson KA, Chen JL. Functional outcome of en bloc excision and osteoarticular allograft replacement with the Sauve-Kapandji procedure for Campanacci grade 3 giant-cell tumor of the distal radius. J Hand Surg Am 2006 Oct;31(8):1340-1348.

(77) Bianchi G, Donati D, Staals EL, Mercuri M. Osteoarticular allograft reconstruction of the distal radius after bone tumour resection. J Hand Surg Br 2005 Aug;30(4):369-373.

(78) Fox EJ, Hau MA, Gebhardt MC, Hornicek FJ, Tomford WW, Mankin HJ. Long-term followup of proximal femoral allografts. Clin Orthop Relat Res 2002 Apr; (397):106-113.

(79) Alho A, Karaharju EO, Korkala O, Laasonen EM, Holmstrom T, Muller C. Allogeneic grafts for bone tumor. 21 cases of osteoarticular and segmental grafts. Acta Orthop Scand 1989 Apr;60(2):143-153.

(80) Mnaymneh W, Malinin TI, Lackman RD, Hornicek FJ, Ghandur-Mnaymneh L. Massive distal femoral osteoarticular allografts after resection of bone tumors. Clin Orthop Relat Res 1994 Jun; (303):103-115.

(81) Mankin HJ, Gebhardt MC, Jennings LC, Springfield DS, Tomford WW. Long-term results of allograft replacement in the management of bone tumors. Clin Orthop Relat Res 1996 Mar; (324):86-97.

(82) Muscolo DL, Ayerza MA, Aponte-Tinao LA, Ranalletta M. Use of distal femoral osteoarticular allografts in limb salvage surgery. J Bone Joint Surg Am 2005 Nov;87(11):2449-2455.

(83) Toy PC, White JR, Scarborough MT, Enneking WF, Gibbs CP. Distal femoral osteoarticular allografts: long-term survival, but frequent complications. Clin Orthop Relat Res 2010 Nov;468(11):2914-2923.

(84) Ogilvie CM, Crawford EA, Hosalkar HS, King JJ, Lackman RD. Long-term results for limb salvage with osteoarticular allograft reconstruction. Clin Orthop Relat Res 2009 Oct;467(10):2685-2690.

(85) Friedlaender GE, Strong DM, Tomford WW, Mankin HJ. Long-term follow-up of patients with osteochondral allografts. A correlation between immunologic responses and clinical outcome. Orthop Clin North Am 1999 Oct;30(4):583-588.

(86) Strong DM, Friedlaender GE, Tomford WW, Springfield DS, Shives TC, Burchardt H, et al. Immunologic responses in human recipients of osseous and osteochondral allografts. Clin Orthop Relat Res 1996 May; (326):107-114.

(87) Friedlaender GE, Strong DM, Sell KW. Studies on the antigenicity of bone. I. Freeze-dried and deep-frozen bone allografts in rabbits. J Bone Joint Surg Am 1976 Sep;58(6):854-858.

(88) Friedlaender GE. Bone allografts: the biological consequences of immunological events. J Bone Joint Surg Am 1991 Sep;73(8):1119-1122.

(89) Hornicek FJ, Gebhardt MC, Tomford WW, Sorger JI, Zavatta M, Menzner JP, et al. Factors affecting nonunion of the allograft-host junction. Clin Orthop Relat Res 2001 Jan; (382):87-98.

(90) Muscolo DL, Ayerza MA, Calabrese ME, Redal MA, Santini Araujo E. Human leukocyte antigen matching, radiographic score, and histologic findings in massive frozen bone allografts. Clin Orthop Relat Res 1996 May; (326):115-126.

(91) Hornicek FJ,Jr, Mnaymneh W, Lackman RD, Exner GU, Malinin TI. Limb salvage with osteoarticular allografts after resection of proximal tibia bone tumors. Clin Orthop Relat Res 1998 Jul; (352):179-186.

(92) Mankin HJ, Hornicek FJ, Raskin KA. Infection in massive bone allografts. Clin Orthop Relat Res 2005 Mar; (432):210-216.

(93) Gebhardt MC, Flugstad DI, Springfield DS, Mankin HJ. The use of bone allografts for limb salvage in high-grade extremity osteosarcoma. Clin Orthop Relat Res 1991 Sep; (270):181-196.

(94) Buck BE, Malinin TI. Human bone and tissue allografts. Preparation and safety. Clin Orthop Relat Res 1994 Jun; (303):8-17.

(95) Lord CF, Gebhardt MC, Tomford WW, Mankin HJ. Infection in bone allografts. Incidence, nature, and treatment. J Bone Joint Surg Am 1988 Mar;70(3):369-376.

(96) Liu JW, Chao LH, Su LH, Wang JW, Wang CJ. Experience with a bone bank operation and allograft bone infection in recipients at a medical centre in southern Taiwan. J Hosp Infect 2002 Apr;50(4):293-297.

(97) Tomford WW. Transmission of disease through transplantation of musculoskeletal allografts. J Bone Joint Surg Am 1995 Nov;77(11):1742-1754.

(98) Schratt HE, Regel G, Lobenhoffer P, Tscherne H. Organization of a bone and tissue bank. Consequences for organization of bone and tissue banks after HIV and hepatitis C infections. Unfallchirurg 1996 Nov;99(11):880-888.

(99) Centers for Disease Control (CDC). Transmission of HIV through bone transplantation: case report and public health recommendations. MMWR Morb Mortal Wkly Rep 1988 Oct 7;37(39):597-599.

(100) Tugwell BD, Patel PR, Williams IT, Hedberg K, Chai F, Nainan OV, et al. Transmission of hepatitis C virus to several organ and tissue recipients from an antibody-negative donor. Ann Intern Med 2005 Nov 1;143(9):648-654.

(101) Conrad EU, Gretch DR, Obermeyer KR, Moogk MS, Sayers M, Wilson JJ, et al. Transmission of the hepatitis-C virus by tissue transplantation. J Bone Joint Surg Am 1995 Feb;77(2):214-224.

(102) Simonds RJ, Holmberg SD, Hurwitz RL, Coleman TR, Bottenfield S, Conley LJ, et al. Transmission of human immunodeficiency virus type 1 from a seronegative organ and tissue donor. N Engl J Med 1992 Mar 12;326(11):726-732.

(103) Eggen BM, Nordbo SA. Transmission of HCV by organ transplantation. N Engl J Med 1992 Feb 6;326(6):411; author reply 412-413.

(104) Brien EW, Terek RM, Healey JH, Lane JM. Allograft reconstruction after proximal tibial resection for bone tumors. An analysis of function and outcome comparing allograft and prosthetic reconstructions. Clin Orthop Relat Res 1994 Jun;(303):116-127.

(105) Busch MP, Eble BE, Khayam-Bashi H, Heilbron D, Murphy EL, Kwok S, et al. Evaluation of screened blood donations for human immunodeficiency virus type 1 infection by culture and DNA amplification of pooled cells. N Engl J Med 1991 Jul 4;325(1):1-5.

(106) Judas F, Teixeira L, Proenca A. Coimbra University Hospitals' bone and tissue bank: twenty-two years of experience. Transplant Proc 2005 Jul-Aug;37(6):2799-2801.

(107) Hejna MJ, Gitelis S. Allograft prosthetic composite replacement for bone tumors. Semin Surg Oncol 1997 Jan-Feb;13(1):18-24.

(108) Zehr RJ, Enneking WF, Scarborough MT. Allograft-prosthesis composite versus megaprosthesis in proximal femoral reconstruction. Clin Orthop Relat Res 1996 Jan; (322):207-223.

(109) Bradish CF, Kemp HB, Scales JT, Wilson JN. Distal femoral replacement by custom-made prostheses. Clinical follow-up and survivorship analysis. J Bone Joint Surg Br 1987 Mar;69(2):276-284.

(110) Zeegen EN, Aponte-Tinao LA, Hornicek FJ, Gebhardt MC, Mankin HJ. Survivorship analysis of 141 modular metallic endoprostheses at early followup. Clin Orthop Relat Res 2004 Mar; (420):239-250.

(111) Kabukcuoglu Y, Grimer RJ, Tillman RM, Carter SR. Endoprosthetic replacement for primary malignant tumors of the proximal femur. Clin Orthop Relat Res 1999 Jan; (358):8-14.

(112) Bickels J, Wittig JC, Kollender Y, Henshaw RM, Kellar-Graney KL, Meller I, et al. Distal femur resection with endoprosthetic reconstruction: a long-term followup study. Clin Orthop Relat Res 2002 Jul; (400):225-235.

(113) Horowitz SM, Glasser DB, Lane JM, Healey JH. Prosthetic and extremity survivorship after limb salvage for sarcoma. How long do the reconstructions last? Clin Orthop Relat Res 1993 Aug; (293):280-286.

(114) Kawai A, Healey JH, Boland PJ, Athanasian EA, Jeon DG. A rotating-hinge knee replacement for malignant tumors of the femur and tibia. J Arthroplasty 1999 Feb;14(2):187-196.

(115) Biau DJ, Larousserie F, Thevenin F, Piperno-Neumann S, Anract P. Results of 32 allograft-prosthesis composite reconstructions of the proximal femur. Clin Orthop Relat Res 2010 Mar;468(3):834-845.

(116) Kocher MS, Gebhardt MC, Mankin HJ. Reconstruction of the distal aspect of the radius with use of an osteoarticular allograft after excision of a skeletal tumor. J Bone Joint Surg Am 1998 Mar;80(3):407-419.

(117) Brigman BE, Hornicek FJ, Gebhardt MC, Mankin HJ. Allografts about the Knee in Young Patients with High-Grade Sarcoma. Clin Orthop Relat Res 2004 Apr; (421):232-239.

(118) Tomford WW, Thongphasuk J, Mankin HJ, Ferraro MJ. Frozen musculoskeletal allografts. A study of the clinical incidence and causes of infection associated with their use. J Bone Joint Surg Am 1990 Sep;72(8):1137-1143.

(119) Rödl RW, Ozaki T, Hoffmann C, Bottner F, Lindner N, Winkelmann W. Osteoarticular allograft in surgery for high-grade malignant tumours of bone. J Bone Joint Surg Br 2000 Sep;82(7):1006-1010.

(120) Farid Y, Lin PP, Lewis VO, Yasko AW. Endoprosthetic and allograft-prosthetic composite reconstruction of the proximal femur for bone neoplasms. Clin Orthop Relat Res 2006 Jan;442:223-229.

(121) Anract P, Coste J, Vastel L, Jeanrot C, Mascard E, Tomeno B. Proximal femoral reconstruction with megaprosthesis versus allograft prosthesis composite. A comparative study of functional results, complications and longevity in 41 cases. Rev Chir Orthop Reparatrice Appar Mot 2000 May;86(3):278-288.

(122) Dick HM, Strauch RJ. Infection of massive bone allografts. Clin Orthop Relat Res 1994 Sep; 306:46-53.

(123) Aspenberg P. Bank bone, infections and HIV. Acta Orthop Scand 1998 Dec;69(6):557-558.

(124) Gitelis S, Mallin BA, Piasecki P, Turner F. Intralesional excision compared with en bloc resection for giant-cell tumors of bone. J Bone Joint Surg Am 1993 Nov;75(11):1648-1655.

(125) Cheng CY, Shih HN, Hsu KY, Hsu RW. Treatment of giant cell tumor of the distal radius. Clin Orthop Relat Res 2001 Feb;(383)(383):221-228.

(126) Harness NG, Mankin HJ. Giant-cell tumor of the distal forearm. J Hand Surg Am 2004 Mar;29(2):188-193.

(127) Vander Griend RA, Funderburk CH. The treatment of giant-cell tumors of the distal part of the radius. J Bone Joint Surg Am 1993 Jun;75(6):899-908.

(128) Roberts P, Chan D, Grimer RJ, Sneath RS, Scales JT. Prosthetic replacement of the distal femur for primary bone tumours. J Bone Joint Surg Br 1991 Sep;73(5):762-769.

(129) Malawer MM, Chou LB. Prosthetic survival and clinical results with use of large-segment replacements in the treatment of high-grade bone sarcomas. J Bone Joint Surg Am 1995 Aug;77(8):1154-1165.

(130) Natarajan MV, Sivaseelam A, Rajkumar G, Hussain SH. Custom megaprosthetic replacement for proximal tibial tumours. Int Orthop 2003;27(6):334-337.

(131) Hanna SA, Sewell MD, Aston WJ, Pollock RC, Skinner JA, Cannon SR, et al. Femoral diaphyseal endoprosthetic reconstruction after segmental resection of primary bone tumours. J Bone Joint Surg Br 2010 Jun;92(6):867-874.

(132) Ruggieri P, Mavrogenis AF, Bianchi G, Sakellariou VI, Mercuri M, Papagelopoulos PJ. Outcome of the intramedullary diaphyseal segmental defect fixation system for bone tumors. J Surg Oncol 2011 Jul 1;104(1):83-90.

(133) Abudu A, Carter SR, Grimer RJ. The outcome and functional results of diaphyseal endoprostheses after tumour excision. J Bone Joint Surg Br 1996 Jul;78(4):652-657.

(134) Aldlyami E, Abudu A, Grimer RJ, Carter SR, Tillman RM. Endoprosthetic replacement of diaphyseal bone defects. Long-term results. Int Orthop 2005 Feb;29(1):25-29.

(135) Ahlmann ER, Menendez LR. Intercalary endoprosthetic reconstruction for diaphyseal bone tumours. J Bone Joint Surg Br 2006 Nov;88(11):1487-1491.

(136) Cannon CP, Paraliticci GU, Lin PP, Lewis VO, Yasko AW. Functional outcome following endoprosthetic reconstruction of the proximal humerus. J Shoulder Elbow Surg 2009 Sep-Oct;18(5):705-710.

(137) Jeys LM, Grimer RJ, Carter SR, Tillman RM. Periprosthetic infection in patients treated for an orthopaedic oncological condition. J Bone Joint Surg Am 2005 Apr;87(4):842-849.

(138) Henderson ER, Groundland JS, Pala E, Dennis JA, Wooten R, Cheong D, et al. Failure mode classification for tumor endoprostheses: retrospective review of five institutions and a literature review. J Bone Joint Surg Am 2011 Mar 2;93(5):418-429.

(139) Muscolo DL, Ayerza MA, Aponte-Tinao LA. Survivorship and radiographic analysis of knee osteoarticular allografts. Clin Orthop Relat Res 2000 Apr; 373:73-79.

(140) Donati D, Giacomini S, Gozzi E, Mercuri M. Proximal femur reconstruction by an allograft prosthesis composite. Clin Orthop Relat Res 2002 Jan; 394:192-200.

(141) Kassab M, Dumaine V, Babinet A, Ouaknine M, Tomeno B, Anract P. Twenty nine shoulder reconstructions after resection of the proximal humerus for neoplasm with mean 7-year follow-up. Rev Chir Orthop Reparatrice Appar Mot 2005 Feb;91(1):15-23.

(142) Potter BK, Adams SC, Pitcher JD,Jr, Malinin TI, Temple HT. Proximal humerus reconstructions for tumors. Clin Orthop Relat Res 2009 Apr;467(4):1035-1041.

(143) Dudkiewicz I, Velkes S, Oran A, Pritsch M, Salai M. Composite grafts in the treatment of osteosarcoma of the proximal humerus. Cell Tissue Bank 2003;4(1):37-41.

(144) Black AW, Szabo RM, Titelman RM. Treatment of malignant tumors of the proximal humerus with allograft-prosthesis composite reconstruction. J Shoulder Elbow Surg 2007 Sep-Oct;16(5):525-533.

(145) Clohisy DR, Mankin HJ. Osteoarticular allografts for reconstruction after resection of a musculoskeletal tumor in the proximal end of the tibia. J Bone Joint Surg Am 1994 Apr;76(4):549-554.

(146) Probyn LJ, Wunder JS, Bell RS, Griffin AM, Davis AM. A comparison of outcome of osteoarticular allograft reconstruction and shoulder arthrodesis following resection of primary tumours of the proximal humerus. Sarcoma 1998;2(3-4):163-170.

(147) Lietman SA, Tomford WW, Gebhardt MC, Springfield DS, Mankin HJ. Complications of irradiated allografts in orthopaedic tumor surgery. Clin Orthop Relat Res 2000 Jun; 375:214-217.

(148) Getty PJ, Peabody TD. Complications and functional outcomes of reconstruction with an osteoarticular allograft after intra-articular resection of the proximal aspect of the humerus. J Bone Joint Surg Am 1999 Aug;81(8):1138-1146.

(149) Zimel MN, Cizik AM, Rapp TB, Weisstein JS, Conrad EU,3rd. Megaprosthesis versus Condyle-sparing intercalary allograft: distal femoral sarcoma. Clin Orthop Relat Res 2009 Nov;467(11):2813-2824.

(150) Berrey BH,Jr, Lord CF, Gebhardt MC, Mankin HJ. Fractures of allografts. Frequency, treatment, and end-results. J Bone Joint Surg Am 1990 Jul;72(6):825-833.

(151) Thompson RC,Jr, Garg A, Clohisy DR, Cheng EY. Fractures in large-segment allografts. Clin Orthop Relat Res 2000 Jan; 370:227-235.

(152) McGoveran BM, Davis AM, Gross AE, Bell RS. Evaluation of the allograft-prosthesis composite technique for proximal femoral reconstruction after resection of a primary bone tumour. Can J Surg 1999 Feb;42(1):37-45.

(153) Deijkers RL, Bloem RM, Kroon HM, Van Lent JB, Brand R, Taminiau AH. Epidiaphyseal versus other intercalary allografts for tumors of the lower limb. Clin Orthop Relat Res 2005 Oct;439:151-160.

(154) San-Julian M, Canadell J. Fractures of allografts used in limb preserving operations. Int Orthop 1998;22(1):32-36.

(155) Chang DW, Weber KL. Use of a vascularized fibula bone flap and intercalary allograft for diaphyseal reconstruction after resection of primary extremity bone sarcomas. Plast Reconstr Surg 2005 Dec;116(7):1918-1925.

(156) Muscolo DL, Ayerza MA, Farfalli G, Aponte-Tinao LA. Proximal tibia osteoarticular allografts in tumor limb salvage surgery. Clin Orthop Relat Res 2010 May;468(5):1396-1404.

(157) Vander Griend RA. The effect of internal fixation on the healing of large allografts. J Bone Joint Surg Am 1994 May;76(5):657-663.

(158) Miller BJ, Virkus WW. Intercalary allograft reconstructions using a compressible intramedullary nail: a preliminary report. Clin Orthop Relat Res 2010 Sep;468(9):2507-2513.

(159) Clarke HD, Berry DJ, Sim FH. Salvage of failed femoral megaprostheses with allograft prosthesis composites. Clin Orthop Relat Res 1998 Nov;356:222-229.

(160) Abdeen A, Hoang BH, Athanasian EA, Morris CD, Boland PJ, Healey JH. Allograft-prosthesis composite reconstruction of the proximal part of the humerus: functional outcome and survivorship. J Bone Joint Surg Am 2009 Oct;91(10):2406-2415.

(161) Wunder JS, Davis AM, Hummel JS, Mandelcorn J, Griffin AM, Bell RS. The effect of intramedullary cement on intercalary allograft reconstruction of bone defects after tumour resection: a pilot study. Can J Surg 1995 Dec;38(6):521-527.

(162) Ozaki T, Hillmann A, Bettin D, Wuisman P, Winkelmann W. Intramedullary, antibiotic-loaded cemented, massive allografts for skeletal reconstruction. 26 cases compared with 19 uncemented allografts. Acta Orthop Scand 1997 Aug;68(4):387-391.

(163) Gerrand CH, Griffin AM, Davis AM, Gross AE, Bell RS, Wunder JS. Large segment allograft survival is improved with intramedullary cement. J Surg Oncol 2003 Dec;84(4):198-208.

(164) Muscolo DL, Ayerza MA, Aponte-Tinao L, Ranalletta M, Abalo E. Intercalary femur and tibia segmental allografts provide an acceptable alternative in reconstructing tumor resections. Clin Orthop Relat Res 2004 Sep;426:97-102.

(165) San Julian Aranguren M, Leyes M, Mora G, Canadell J. Consolidation of massive bone allografts in limb-preserving operations for bone tumours. Int Orthop 1995;19(6):377-382.

(166) Langlais F, Lambotte JC, Collin P, Thomazeau H. Long-term results of allograft composite total hip prostheses for tumors. Clin Orthop Relat Res 2003 Sep;414:197-211.

(167) Harris AI, Gitelis S, Sheinkop MB, Rosenberg AG, Piasecki P. Allograft prosthetic composite reconstruction for limb salvage and severe deficiency of bone at the knee or hip. Semin Arthroplasty 1994 Apr;5(2):85-94.

(168) Asavamongkolkul A, Waikakul S, Phimolsarnti R, Kiatisevi P. Functional outcome following excision of a tumour and reconstruction of the distal radius. Int Orthop 2009 Feb;33(1):203-209.

(169) Gilbert NF, Yasko AW, Oates SD, Lewis VO, Cannon CP, Lin PP. Allograft-prosthetic composite reconstruction of the proximal part of the tibia. An analysis of the early results. J Bone Joint Surg Am 2009 Jul;91(7):1646-1656.

(170) Wunder JS, Leitch K, Griffin AM, Davis AM, Bell RS. Comparison of two methods of reconstruction for primary malignant tumors at the knee: a sequential cohort study. J Surg Oncol 2001 Jun;77(2):89-99; discussion 100.

(171) Wilkins RM, Kelly CM. Revision of the failed distal femoral replacement to allograft prosthetic composite. Clin Orthop Relat Res 2002 Apr;397:114-118.

(172) Muscolo DL, Ayerza MA, Aponte-Tinao LA, Ranalletta M. Partial epiphyseal preservation and intercalary allograft reconstruction in high-grade metaphyseal osteosarcoma of the knee. J Bone Joint Surg Am 2004 Dec;86-A(12):2686-2693.

(173) Biau DJ, Davis A, Vastel L, Tomeno B, Anract P. Function, disability, and health-related quality of life after allograft-prosthesis composite reconstructions of the proximal femur. J Surg Oncol 2008 Mar 1;97(3):210-215.

(174) Gitelis S, Piasecki P. Allograft prosthetic composite arthroplasty for osteosarcoma and other aggressive bone tumors. Clin Orthop Relat Res 1991 Sep;270:197-201.

(175) Mercuri M, Capanna R, Manfrini M, Bacci G, Picci P, Ruggieri P, et al. The management of malignant bone tumors in children and adolescents. Clin Orthop Relat Res 1991 Mar;264:156-168.

(176) Dubousset J, Missenard G, Kalifa C. Management of osteogenic sarcoma in children and adolescents. Clin Orthop Relat Res 1991 Sep;270:52-59.

(177) Yang YF, Zhang GM, Xu ZH, Wang JW. Homeochronous usage of structural bone allografts with vascularized fibular autografts for biological repair of massive bone defects in the lower extremities after bone tumor excision. J Reconstr Microsurg 2010 Feb;26(2):109-115.

(178) Ozaki T, Hillmann A, Wuisman P, Winkelmann W. Reconstruction of tibia by ipsilateral vascularized fibula and allograft. 12 cases with malignant bone tumors. Acta Orthop Scand 1997 Jun;68(3):298-301.

(179) Bernd L, Sabo D, Zahlten-Hinguranage A, Niemeyer P, Daecke W, Simank HG. Experiences with vascular pedicled fibula in reconstruction of osseous defects in primary malignant bone tumors. Orthopade 2003 Nov;32(11):983-993.

(180) Hennen J, Sabo D, Martini AK, Bernd L. Mantel transplant for defect reconstruction after resection of malignant bone tumors of the lower extremity. Unfallchirurg 2002 Feb;105(2):120-127.

(181) Moran SL, Shin AY, Bishop AT. The use of massive bone allograft with intramedullary free fibular flap for limb salvage in a pediatric and adolescent population. Plast Reconstr Surg 2006 Aug;118(2):413-419.

(182) Abed YY, Beltrami G, Campanacci DA, Innocenti M, Scoccianti G, Capanna R. Biological reconstruction after resection of bone tumours around the knee: long-term follow-up. J Bone Joint Surg Br 2009 Oct;91(10):1366-1372.

(183) Innocenti M, Abed YY, Beltrami G, Delcroix L, Manfrini M, Capanna R. Biological reconstruction after resection of bone tumors of the proximal tibia using allograft shell and intramedullary free vascularized fibular graft: long-term results. Microsurgery 2009;29(5):361-372.

(184) Li J, Wang Z, Guo Z, Chen GJ, Li SW, Pei GX. The use of massive allograft with intramedullary fibular graft for intercalary reconstruction after resection of tibial malignancy. J Reconstr Microsurg 2011 Jan;27(1):37-46.

(185) Jager T, Journeau P, Dautel G, Barbary S, Haumont T, Lascombes P. Is combining massive bone allograft with free vascularized fibular flap the children's reconstruction answer to lower limb defects following bone tumour resection? Orthop Traumatol Surg Res 2010 Jun;96(4):340-347.

(186) Li J, Wang Z, Guo Z, Chen GJ, Fu J, Pei GX. The use of allograft shell with intramedullary vascularized fibula graft for intercalary reconstruction after diaphyseal resection for lower extremity bony malignancy. J Surg Oncol 2010 Oct 1;102(5):368-374.

(187) Capanna R, Campanacci DA, Belot N, Beltrami G, Manfrini M, Innocenti M, et al. A new reconstructive technique for intercalary defects of long bones: the association of massive allograft with vascularized fibular autograft. Long-term results and comparison with alternative techniques. Orthop Clin North Am 2007 Jan;38(1):51-60, vi.

(188) Ramseier LE, Malinin TI, Temple HT, Mnaymneh WA, Exner GU. Allograft reconstruction for bone sarcoma of the tibia in the growing child. J Bone Joint Surg Br 2006 Jan;88(1):95-99.

(189) Muscolo DL, Ayerza MA, Calabrese ME, Gruenberg M. The use of a bone allograft for reconstruction after resection of giant-cell tumor close to the knee. J Bone Joint Surg Am 1993 Nov;75(11):1656-1662.

(190) Manfrini M, Gasbarrini A, Malaguti C, Ceruso M, Innocenti M, Bini S, et al. Intraepiphyseal resection of the proximal tibia and its impact on lower limb growth. Clin Orthop Relat Res 1999 Jan;358:111-119.

(191) Ceruso M, Taddei F, Bigazzi P, Manfrini M. Vascularised fibula graft inlaid in a massive bone allograft: considerations on the bio-mechanical behaviour of the

combined graft in segmental bone reconstructions after sarcoma resection. Injury 2008 Sep;39 Suppl 3:S68-74.

(192) Chang DW, Weber KL. Segmental femur reconstruction using an intercalary allograft with an intramedullary vascularized fibula bone flap. J Reconstr Microsurg 2004 Apr;20(3):195-199.

(193) Ono H, Yajima H, Mizumoto S, Miyauchi Y, Mii Y, Tamai S. Vascularized fibular graft for reconstruction of the wrist after excision of giant cell tumor. Plast Reconstr Surg 1997 Apr;99(4):1086-1093.

(194) Hatano H, Morita T, Kobayashi H, Otsuka H. A ceramic prosthesis for the treatment of tumours of the distal radius. J Bone Joint Surg Br 2006 Dec;88(12):1656-1658.

(195) Sheth DS, Healey JH, Sobel M, Lane JM, Marcove RC. Giant cell tumor of the distal radius. J Hand Surg Am 1995 May;20(3):432-440.

(196) Natarajan MV, Chandra Bose J, Viswanath J, Balasubramanian N, Sameer M. Custom prosthetic replacement for distal radial tumours. Int Orthop 2009 Aug;33(4):1081-1084.

(197) Muramatsu K, Ihara K, Azuma E, Orui R, Goto Y, Shigetomi M, et al. Free vascularized fibula grafting for reconstruction of the wrist following wide tumor excision. Microsurgery 2005;25(2):101-106.

(198) Aithal VK, Bhaskaranand K. Reconstruction of the distal radius by fibula following excision of giant cell tumor. Int Orthop 2003;27(2):110-113.

(199) Minami A, Kato H, Iwasaki N. Vascularized fibular graft after excision of giant-cell tumor of the distal radius: wrist arthroplasty versus partial wrist arthrodesis. Plast Reconstr Surg 2002 Jul;110(1):112-117.

(200) Innocenti M, Delcroix L, Balatri A. Vascularized growth plate transfer for distal radius reconstruction. Semin Plast Surg 2008 Aug;22(3):186-194.

(201) Maruthainar N, Zambakidis C, Harper G, Calder D, Cannon SR, Briggs TW. Functional outcome following excision of tumours of the distal radius and reconstruction by autologous non-vascularized osteoarticular fibula grafting. J Hand Surg Br 2002 Apr;27(2):171-174.

(202) GOLD AM. Use of a Prosthesis for the Distal Portion of the Radius Following Resection of a Recurrent Giant-Cell Tumor. J Bone Joint Surg Am 1965 Jan;47:216-218.

(203) GOLD AM. Use of a prosthesis for the distal portion of the radius following resection of a recurrent giant-cell tumor. J Bone Joint Surg Am 1957 Dec;39-A(6):1374-1380.

(204) Ahlmann ER, Menendez LR, Kermani C, Gotha H. Survivorship and clinical outcome of modular endoprosthetic reconstruction for neoplastic disease of the lower limb. J Bone Joint Surg Br 2006 Jun;88(6):790-795.

(205) Myers GJ, Abudu AT, Carter SR, Tillman RM, Grimer RJ. The long-term results of endoprosthetic replacement of the proximal tibia for bone tumours. J Bone Joint Surg Br 2007 Dec;89(12):1632-1637.

(206) Flint MN, Griffin AM, Bell RS, Ferguson PC, Wunder JS. Aseptic loosening is uncommon with uncemented proximal tibia tumor prostheses. Clin Orthop Relat Res 2006 Sep;450:52-59.

(207) Schwartz AJ, Kabo JM, Eilber FC, Eilber FR, Eckardt JJ. Cemented endoprosthetic reconstruction of the proximal tibia: how long do they last? Clin Orthop Relat Res 2010 Nov;468(11):2875-2884.

(208) Schwartz AJ, Kabo JM, Eilber FC, Eilber FR, Eckardt JJ. Cemented distal femoral endoprostheses for musculoskeletal tumor: improved survival of modular versus custom implants. Clin Orthop Relat Res 2010 Aug;468(8):2198-2210.

(209) Torbert JT, Fox EJ, Hosalkar HS, Ogilvie CM, Lackman RD. Endoprosthetic reconstructions: results of long-term followup of 139 patients. Clin Orthop Relat Res 2005 Sep;438:51-59.

(210) Donati D, Colangeli M, Colangeli S, Di Bella C, Mercuri M. Allograft-prosthetic composite in the proximal tibia after bone tumor resection. Clin Orthop Relat Res 2008 Feb;466(2):459-465.

(211) Hirn M. Long intramedullary stems of prosthetic components reduce complications, when allograft-prosthesis composite is used in tumor reconstruction. J Surg Oncol 2002 Mar;79(3):201-203.

(212) Jofe MH, Gebhardt MC, Tomford WW, Mankin HJ. Reconstruction for defects of the proximal part of the femur using allograft arthroplasty. J Bone Joint Surg Am 1988 Apr;70(4):507-516.

# 4 List of figures

# 5 List of tables

# 6 Appendix

## 6.1 Curriculum vitae

*Angaben zur Person:*

| | |
|---|---|
| Name, Vorname | **Rabitsch Katharina** |
| Geboren am | 29.04.1987 |
| Geburtsort | Graz |
| Staatsangehörigkeit | Österreich |
| Familienstand | Ledig |

*Schulbildung:*

| | |
|---|---|
| 06/2005 | Matura am Bundesgymnasium Kirchengasse, Graz |
| 1997 - 2005 | Bundesgymnasium Kirchengasse, Graz |
| 1993 - 1997 | Karl-Morre Volksschule, Graz |

*Ausbildung:*

| | |
|---|---|
| 01/2012 | Abschluss des 3. Studienabschnittes Humanmedizin |
| 05/2010 | Abschluss des 2. Studienabschnittes Humanmedizin |
| 07/2006 | Abschluss des 1. Studienabschnittes Humanmedizin |

| | |
|---|---|
| Diplomarbeit: | |
| Originaltitel: | Allograft reconstruction in the treatment of musculoskeletal tumours – a comparative analysis |
| Ausgeführt an der | Medizinischen Universität Graz |
| Betreuer: | OA. Dr. Werner Maurer-Ertl<br>*Universitätsklinik für Orthopädie* |
| | ao. Univ. Prof. Dr. Andreas Leithner<br>*Universitätsklinik für Orthopädie* |
| Praktisches Jahr: | |
| 12/2010 | 3. Fächergruppe, LKH Graz 5 Wochen<br>Augenheilkunde |
| 10/2010 | 1. Fächergruppe, LKH Graz 10 Wochen<br>Orthopädie |
| 07/2010 | 2. Fächergruppe, Klinikum Passau 6 Wochen<br>Innere Medizin, Onkologie |
| 06/2010 | Allgemeinmedizin, Fohnsdorf 5 Wochen<br>Praxis Dr. Seitlinger |
| *Famulaturen:* | |
| 2010 | Krankenhaus der Barmherzigen Brüder, Graz<br>Allgemeinchirurgie 4 Wochen |
| 2009 | LKH Judenburg<br>Unfallchirurgie 4 Wochen |
| 2008 | Krankenhaus der Barmherzigen Brüder, Graz<br>Innere Medizin 4 Wochen |
| 2007 | Univ. Klinik für Kinderchirurgie, Graz<br>Kinderchirurgie 4 Wochen |