Autologous morsellised bone grafting restores uncontained femoral bone defects in knee arthroplasty

AN IN VIVO STUDY IN HORSES

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The properties of impacted morsellised bone graft (MBG) in revision total knee arthroplasty (TKA) were studied in 12 horses. The left hind metatarsophalangeal joint was replaced by a human TKA. The horses were then randomly divided into graft and control groups. In the graft group, a unicompartmental, lateral uncontained defect was created in the third metatarsal bone and reconstructed using autologous MBG before cementing the TKA. In the control group, a cemented TKA was implanted without the bone resection and grafting procedure. After four to eight months, the animals were killed and a biomechanical loading test was performed with a cyclic load equivalent to the horse's body-weight to study mechanical stability. After removal of the prosthesis, the distal third metatarsal bone was studied radiologically, histologically and by quantitative and micro CT.

Biomechanical testing showed that the differences in deformation between the graft and the control condyles were not significant for either elastic or time-dependent deformations. The differences in bone mineral density (BMD) between the graft and the control condyles were not significant. The BMD of the MBG was significantly lower than that in the other regions in the same limb. Micro CT showed a significant difference in the degree of anisotropy between the graft and host bone, even although the structure of the area of the MBG had trabecular

orientation in the direction of the axial load.

Histological analysis revealed that all the grafts were revascularised and completely incorporated into a new trabecular structure with few or no remnants of graft. Our study provides a basis for the clinical application of this technique with MBG in revision TKA.

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In total knee arthroplasty (TKA), the distal femoral bone stock may in time be compromised because of either stress shielding¹⁻⁴ or osteolysis induced by wear particles.⁵⁻⁷ These femoral bone defects are often uncontained and pose serious problems during revision surgery. Reconstruction is required to compensate for the loss of bone stock. Many surgeons prefer reconstruction using bone-grafting techniques.⁸⁻¹² In general, impaction bone grafting with morsellised bone grafts (MBG) is aimed at restoration of the bone loss generated around the components of the prosthesis. Most studies on the use of MBG for reconstruction of femoral and acetabular bone defects in revision total hip arthroplasty (THA) have reported favourable results.¹³⁻¹⁵ Wire meshes are used to create containment for the MBG in cases of uncontained bone defects in revision THA.¹⁵ In TKA, meshes are less easily applied since the soft-tissue coverage is often insufficient. Therefore a grafting technique for reconstruction of uncontained femoral bone defects with MBG (without meshes) has been developed.

Our aim was to investigate in vivo the biomechanical, radiological and histological properties of autologous MBG used for the reconstruction of uncontained femoral bone defects in TKA in an equine model.

Materials and Methods

Operative technique. We used 14 healthy, skeletally mature Dutch Warmblood Horses. Two animals were subsequently excluded. One with a stable reconstruction died three days after surgery because of septic colitis and the other was killed six weeks after operation because of severe collateral instability of the operated joint. Twelve horses (4 female, 8 male) with a mean body-weight of 540 ± 45 kg remained.

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Table I. Details of the 12 horses which had replacement of the left hind MTP joint by a human TKA

Horse	Gender	Body-weight (kg)	Group	Killed (mth)
1	M	549	Control	6
2	M	510	Graft	6
3	M	530	Control	8
4	F	503	Graft	8
5	M	510	Graft	8
6	M	474	Control	4
7	F	580	Graft	4
8	M	516	Control	6
9	M	624	Graft	6
10	M	580	Control	8
11	F	520	Graft	6
12	F	594	Control	6

Fig. 1

Anterior intraoperative view of the left hind MTP joint after bone resection for a posterior stabilised TKA with the horse lying on its right side. A standard lateral uncontained bone defect has been created in the third metatarsal bone.

We had already performed a pilot study of replacing the metatarsophalangeal (MTP) joint in one horse without the bone-grafting procedure.¹⁶ The local animal care committee gave full approval for the research project.

All the operations were performed by one surgeon (MCWM). In an operating room under aseptic conditions and under general anaesthesia the animal was placed on its right side. Intravenous antibiotic prophylaxis had been given before surgery. The left hind limb was prepared for surgery with a tourniquet above the level of the MTP joint and an anterior approach was used to expose the joint. Using modified resection guide instruments, the distal epiphysis of the third metatarsal bone and the proximal first phalanx were prepared to fit a human unstemmed 52 mm cruciate-sacrificing implant (Insall Burstein Posterior Stabilized; Johnson & Johnson, Raynham, Massachusetts). The spine of the polyethylene part of the tibial component was removed to reduce the motion constraint.

The horses were then randomly divided into two groups: control and graft (Table I). In the graft group a standard uncontained bone defect of 1 cm, with a volume of 3.4 cm³

Fig. 2

Diagram of the experimental apparatus for the loading tests A and B (anterior view). An axial cyclical load is applied without a tibial component in an upside-down position, to the lateral part of the femoral component. Elastic and time-dependent deformation is measured by two extensometers (resolution, 8 µm) (A, clamp fixed to the test bank; B, distal metatarsal bone in an upside-down position cemented in the clamp; C, femoral component; D, extensometer; E, MTS loading machine applying axial load through a peg.

(Fig. 1), was created by removing the most distal part of the lateral metatarsal bone. Autologous trabecular MBG was taken from the tuber coxae with a gouge and morsellised into chips 0.5 cm³ in size. A plastic sheet was placed between the trial femoral component and the defect. The MBG was firmly impacted into the defect by hand using a punch while the trial femoral component was in situ. The femoral component was carefully removed after impaction while the plastic sheet prevented disturbance or collapse of the MBG. The definite femoral and tibial components were cemented with the MBG in place after removal of the plastic sheet. In the control group, the MTP joint was replaced by a TKA without the bone resection and bone-grafting procedure. For both groups, a supportive cast was applied for a period of six weeks. Approximately 30 minutes after recovery from surgery, the horses walked from the recovery unit to their boxes, bearing full weight on the operated limb. They were kept in stables, and after removal of the cast were allowed to walk at hand outside the boxes daily. A low dose of a non-steroid anti-inflammatory drug was administered daily until the animals were killed at 4, 6

Fig. 3

Lateral view of a distal metatarsal bone in an upside-down position after impact of a MBG and placement of a cemented femoral component immediately after operation. The metatarsal bone is cemented into a clamp for cyclical axial loading.

or 8 months after the operation (Table I).

Biomechanical loading test. After killing, the left and right third metatarsal bones were kept on ice for 12 hours. They were then stripped free of all soft tissues. The left distal metatarsal bone was potted in bone cement and clamped in an upside-down position in a testing machine (MTS model 458020; Systems Corporation, Minneapolis, Minnesota). A cyclical axial load with a frequency of 1 Hz was applied to the lateral part of the femoral component (test A, Fig. 2). Loading with a compressive force of 40%, 80% and 100% of the horse's body-weight was performed for three periods of 30 minutes, respectively. Metatarsal deformation and displacement were determined by measuring the elastic and the time-dependent deformation between the prosthesis and bone at the medial and lateral sides using extensometers with a resolution of 8 μm . The extensometers were aligned in the axial direction where maximal deformation was expected. Elastic deformation was defined as the local displacement during each loading cycle between the distal metatarsal bone and the prosthesis as measured by the extensometers. Time-dependent deformation was defined as the ongoing change of local displacement in time.

To test the immediate postoperative situation, the identical operation was performed in vitro in a laboratory on the contralateral hind third metatarsal bone, replacing the distal part with a cemented femoral component. In the graft group, the same bone defect as in the situation in vivo was

Fig. 4

Diagram of the anterior view of both distal metatarsal bones in an upside-down position after removal of the femoral components and cement. Region 1 is the area with MBG in the graft group, region 7 is the corresponding contralateral area.

Fig. 5

Median elastic deformation with minimum and maximum values at the lateral condyle of the distal metatarsal bones of the graft ($n = 6$) v the control group ($n = 6$) during cyclical axial loading with 100% body-weight for 30 minutes (test A). The deformation was measured by extensometers (resolution, 8 μm).

Fig. 6

Median elastic deformation with minimum and maximum values at the lateral condyle of the distal metatarsal bones of the graft ($n = 6$) v control group ($n = 6$) during cyclical axial loading with 100% body-weight for 30 minutes (test B, immediate postoperative situation). The deformation was measured by extensometers (resolution, 8 μm).

created and reconstructed with MBG taken from the tuber coxae in the same way as was done in the operating room (Fig. 3). In the control group, replacement was carried out without the bone resection and grafting procedure. The previously described loading experiment was performed for the right hind third metatarsal bone in both groups (immediate postoperative situation, test B).

After testing, the bone was fixed in a 4% phosphate-buffered formalin solution for two weeks. The femoral component and cement were removed by immersion in 100% acetone without damage to the bone or interface.

Radiological analysis. A plain anteroposterior radiograph of each left hind metatarsal bone was taken after removal of the femoral component to evaluate the incorporation and trabecular orientation of the MBG.

Quantitative CT. The four metatarsal condyles of each horse were sawn into three parts after marking of the graft region and were kept in 0.1M phosphate-buffered 4% formaldehyde at pH 7.4. The bone mineral density (BMD) of a total of eight regions of interest was determined by QCT (Stratec XCT 960A PQCT; Stratec Medical, Oberdorf, Switzerland) from bone samples of the posterior third part of the condyles. The eight regions of interest for each horse, four in the left and four in the right distal metatarsal bone, comprised the graft and corresponding contralateral distal areas and the more proximal host bone (Fig. 4).

Micro CT. Bone samples, $11 \times 11 \times 15$ mm in size, from the posterior third part of the MBG regions and the more proximal host bone were placed in a cylindrical perspex sample holder and scanned through 360° by micro CT (Scanco Medical Micro CT 20; Scanco Medical, Bassersdorf, Switzerland) with a resolution of 17.4 μm to determine the trabecular architecture and to quantify the degree of anisotropy. From the scanned bone samples, a three-dimensional reconstruction, $8 \times 8 \times 7$ mm in size, was made for the measurements and a threshold of 210 was chosen. The mean intercept length tensor generated an ellipsoid in three perpendicular planes when plotted as the radius at the angle of measurement. The ratios of the eigen

values of the tensor determined the trabecular orientation.¹⁷

Histological analysis. The anterior and middle thirds of the condyles were used for light microscopy. Non-decalcified thin sections were made which were stained with Goldner-Masson. The samples were embedded in PMMA, sectioned into slices of 50 μm with a rotating water-cooled diamond saw and coverslipped unstained or lightly counterstained with basic fuchsin. The remaining parts were decalcified in 25% EDTA, embedded in PMMA, sectioned into slices of 7 μm with a rotatory microtome, and stained with haematoxylin and eosin.

Statistical analysis. Comparisons of the biomechanical and quantitative CT data between the graft and control specimens were performed using the Mann-Whitney test. The Wilcoxon signed-rank test was used to determine differences between the left and right limbs. Friedman's ANOVA was used for quantitative micro and CT measurements in the same animals. P values of less than 0.05 were considered to be significant. Spearman's coefficient was used for correlation measurements between deformation and the time to killing and between BMD and the time to killing.

Results

Clinical observations. The 12 horses tolerated the operation well. Their weight-bearing gait patterns were not entirely symmetrical after removal of the cast, but severe limping was not observed. None showed clinical signs of infection or instability of the joint. Macroscopically, slight damage to the polyethylene tibial inserts was noted in all cases after killing.

Biomechanical findings. In test A, under 100% body-weight loading, the differences in deformation between the graft and the control groups were not significant for elastic deformation (lateral condyle, $p = 0.52$; medial condyle, $p = 0.87$) and time-dependent deformation (lateral condyle, $p = 0.75$, medial condyle, $p = 1.0$). In test B the resistance to loading in the graft group was significantly less imme-

Fig. 7

AP radiograph of a left distal metatarsal bone (case 5), eight months after impaction of a MBG at the lateral condyle. The MBG shows signs of consolidation to the host bone. The junction of the graft and the host bone is still visible.

diately after operation. With 100% body-weight loading, the differences in deformation between the graft and control group were significant for elastic deformation (lateral condyle, $p = 0.01$; medial condyle, $p = 0.006$, respectively) and time-dependent deformation (both condyles, $p = 0.006$). The correlation between deformation and time to killing was weak (elastic deformation of the lateral condyle; $R = 0.21$). The MBG did not collapse under loading with 100% of body-weight during test B. Figures 5 and 6 show the course of the median elastic deformation with minimum and maximum values in time for tests A and B, respectively.

Radiological findings. After four to eight months, the trabecular orientation of the grafts was identical to that in the host bone. Even although the grafted areas could be distinguished from the host bone, all the MBGs showed signs of consolidation to it (Fig. 7).

Quantitative CT findings. The BMD of each of the eight selected regions did not differ significantly between the graft and control groups ($p > 0.05$, Table II) with the exception of the immediate postoperative appearance of the MBG ($p = 0.0039$). In the graft group after four to eight months, the BMD of the MBG was significantly lower than that of the other regions in the same limb ($p = 0.029$). There was no correlation between the BMD of the MBG and the time to sacrifice ($R = 0.13$).

Micro CT findings. The regions of the MBG showed trabecular patterns orientated in the direction of axial loading. The difference in the degree of anisotropy between the samples of the MBG and host bone was significant ($p = 0.025$).

Histological findings. In the non-grafted condyles, the distal bone near the cement-bone interface showed a thin layer (approximately 500 μm) of necrotic bone, which was partly remodelled by creeping substitution into living bone after four months (Fig. 8A). After longer periods of follow-up, the remnants of necrotic bone were scarce. At the

cement-bone interface, the penetration of the cement into the relatively compact subchondral bone was minimal. In some areas, the bone was in direct contact with the prosthesis. Occasionally, a thin layer of non-mineralised osteoid was present at this interface. If a soft-tissue interface was present, it was of varying thickness and consisted of dense fibrous or fibrocartilaginous tissue with a few macrophages (Figs 8A and 8B). The bone directly facing the layer of cement showed signs of intense remodelling. There was a large amount of osteoid and rows of active osteoblasts were present. In some other locations, osteoclastic bone resorption was found (Figs 8C and 8D).

In the grafted condyles, the junction of the MBG with the host bone was difficult to recognise in most sections because of complete consolidation and incorporation of the graft. In fuchsin-stained thick sections, the transition from host to graft was apparent by the change in colour of the younger incorporated graft bone and by a slight change in trabecular architecture (Fig. 8E). In the haematoxylin and eosin sections, the resection plane and also the interface of the host with the graft were stained as a reversal line (Fig. 8H). Signs of this resection plane were found in trabecular bone of normal appearance (Figs 8F to 8J). The MBG itself was completely incorporated into a new trabecular structure. The density of the trabecular bone seemed to match that of the underlying original host bone. Remnants of the grafts were already scarce after four months and were not found at all in the reconstructions with a follow-up period of six or eight months. The incorporated bone was initially a mixture of woven bone and remodelled lamellar bone (Figs 9A to 9C). Close to the cement-bone interface, more woven bone was found, particularly in the four-month specimens (Figs 9D to 9E). Revascularisation and incorporation of the reconstruction had progressed up to the graft-cement interface. Penetration of cement into the graft was much greater than in non-grafted bones (Figs 9F to 9G). After four months, there was formation of bone and small areas of necrotic non-incorporated graft. At most locations, new bone directly contacted the cement without interposition of a soft-tissue interface. In general, if present, the soft-tissue interface was thinner compared with that of non-grafted bones (Fig. 9G). After six and eight months, areas of non-incorporated graft were extremely scarce.

Discussion

A long-term threat to the durability of joint replacements is periprosthetic bone resorption. Solid bone grafting for uncontained bone defects in revision TKA has been applied with good medium-term results.^{10,11} Most reports of impacted MBG in revision THA yielded excellent results,¹³⁻¹⁵ although in two recent studies a high percentage of subsidence of the femoral component was found.^{18,19} On the basis of the results in revision THA it is tempting to use a similar grafting technique in revision TKA. The revascularisation potential of MBG in TKA,

Fig. 8

Figures 8A to 8D – Details of the interface of a non-grafted condyle with implant. The cement has been removed for histotechnical reasons. Figure 8A – A thin layer of fibrocartilaginous tissue (FC) after four months of follow-up. There are small areas of necrosis (N) and new bone (NB) (haematoxylin and eosin $\times 90$). Figure 8B – The same interface after six months ($\times 90$). Figure 8C – The reactive fibrous interface after eight months ($\times 90$). Figure 8D – An enlargement of Figure 8C. There are many osteoblasts in the bone directly under the interface ($\times 180$). Figure 8E – Low magnification section of a reconstructed condyle. There is a change in colour (arrow points) at the location of the interface of host bone with graft bone (upper part) (C, cement penetration in grafted area) fuchsin $\times 10$). Figures 8F to J – The interface of host bone (lower part of figures) with incorporated graft bone in a four-month specimen. Figure 8F – Higher magnification of the interface of the host bone (lower part) with graft bone (upper part). The arrow points at the original resection plane. Figure 8G – The same in polarised light. The bone has a normal lamellar appearance ($\times 70$). Figures 8H and 8J – Higher magnification of the interface. There is a sharp transition from the lamellar bone of the host to the woven bone of the incorporated graft bone ($\times 180$).

Fig. 9

Figures 9A to 9E – Bone after incorporation in the grafted area. Figure 9A – A remnant of the graft (G) encapsulated by new bone (NB) (haematoxylin and eosin $\times 53$). Figure 9B – Incorporated bone under polarised light. There is a normal lamellar appearance ($\times 44$). Figure 9C – The same section under normal light. There is complete incorporation of the graft into normal appearing trabecular bone (haematoxylin and eosin). Figure 9D – Newly formed woven bone (WB) near the cement-bone interface in a four-month specimen (haematoxylin and eosin $\times 105$). Figure 9E – The same section under polarised light. There is irregular orientation of collagen bundles. Figure 9F – The graft-cement interface in a six-month specimen. The graft has been completely incorporated into new normal looking lamellar bone with normal medullary tissue (MT). At many locations the new bone is in direct contact with the cement layer (C, removed during histotechnical processing). At other locations there is a very thin fibrous interface between new bone and cement ($\times 44$). Figure 9G – Higher magnification of the interface of cement with incorporated graft. The arrows point to the thin soft-tissue interface. The bone at this location contains some necrotic remnants of the graft (N) and is partly woven bone (WB) and partly lamellar bone ($\times 156$).

Table II. BMD (mg/cm³) of the metatarsal condyles of 12 horses after removal of the femoral component of a TKA measured by quantitative CT

Horse	Group	Regions							
		1	2	3	4	5	6	7	8
1	Control	695.7	601.8	616.7	538.4	782.3	669.8	669.8	805.5
2	Graft	532.1	500.7	547.7	484.2	701.5	573.6	316.5	667.5
3	Control	716.6	523.6	752.6	627.4	695.3	669.6	713.5	757.6
4	Graft	770.0	686.9	763.0	689.7	852.7	752.7	504.6	737.7
5	Graft	604.2	779.1	889.9	736.1	773.1	766.6	503.5	735.0
6	Control	630.6	628.0	636.9	599.0	659.5	642.6	716.9	763.8
7	Graft	732.6	817.8	908.3	785.1	810.2	699.1	459.9	778.8
8	Control	675.7	507.2	589.7	518.5	718.1	639.8	595.9	690.7
9	Graft	643.4	790.8	856.4	713.2	925.3	761.8	357.7	752.5
10	Control	617.4	524.5	937.2	818.6	679.3	548.6	610.4	707.7
11	Graft	350.1	518.6	638.9	614.5	779.2	667.6	486.0	667.3
12	Control	805.6	725.9	866.7	716.0	792.9	694.0	793.2	705.9

however, may be less than that in THA due to the smaller proximal bone bed. Another disadvantage of MBG may be the lack of containment compared with a structural graft. MBG used for reconstruction of unicondylar uncontained femoral bone loss in a cadaver experiment improved the structural resistance against loading to some extent.²⁰

Biomechanical studies and histological examination of bone grafts in retrieved specimens and animal models are the only methods to evaluate accurately the status of bone grafts. Parks and Engh²¹ studied nine retrieved structural bone grafts used in TKA with a mean follow-up of 41 months. All the allografts were found to be intact and new bone had been laid down on the scaffold of dead bone. Revascularisation and remodelling, however, had not occurred which suggests that, within the follow-up period, a new vital bone structure with the characteristics of the host bone had not been created by this technique of bone grafting. Application of stemmed femoral components was advised to protect the grafts from failure.

The MTP joint of the horse is a large joint which can be fitted with a small-size human TKA. Although the equine MTP joint includes a plantar sesamoid bone instead of a patella and the joint is axially loaded in slight hyperextension, there are functional similarities to the human knee. Despite the anatomical differences and the relatively high body-weight of the horse, we consider replacement of the MTP joint with a human TKA to be a suitable model for an animal study in vivo with MBG in cemented TKA.¹⁷ Since partial weight-bearing is impossible in horses, we chose a relatively small unicondylar, uncontained bone defect because the loading in horses in vivo is extremely high and failure could easily have occurred if larger defects had been created. The elastic and time-dependent deformations observed may not represent the complete range of deformation which may occur as a result of loading modes of the horse MTP joint in vivo during daily activities. Nevertheless, our findings indicate that, at four to eight months after surgery, the structural resistance of the MBG against loading was comparable with that of a control group. In the immediate postoperative situation, however, the elastic deformation of the graft group was significantly

greater. This suggests that a gradual improvement in prosthetic stability had occurred during the follow-up period which resulted in a grafted condyle with biomechanical characteristics as compared with a non-grafted condyle.

Loading itself may be an important factor in the process of graft incorporation. Lamerigts et al²² studied the incorporation of MBG under controlled loading with a subcutaneous pressure implant in goats. Histologically, the initial repair process did not differ between unloaded specimens and specimens loaded with 2 MPa or 4 MPa. After three months, however, the remodelling process following incorporation was more advanced in the specimens loaded with either 2 MPa or 4 MPa compared with the unloaded specimens. The specimens in the 4 MPa group had the highest BMD of the three groups. Thus, high loading results in a high BMD, but slower bone remodelling. These findings suggest that loading is not important in early graft repair but is essential in later remodelling.

The quantitative data suggest that mineralisation occurs during the incorporation process since the BMD of the MBG was greater at the time of sacrifice as compared with the immediate postoperative period. The relatively late occurrence of isotropic features in the remodelling process would explain the significant difference in the degree of anisotropy between the MBG and the host bone.

The histological analysis showed that the MBG had been incorporated into a new trabecular structure with minimal remnants of the grafts. The woven bone had completely remodelled into vital lamellar bone within six to eight months. Our findings support the histological results reported in animal and retrieval studies of MBG in revision THA in vivo. In a goat model for revision THA, MBG was incorporated into the host bone with a good interlock between the host trabecular bone and the graft.^{23,24} In a histological study of eight retrieved acetabular MBGs in cemented revision THA, Buma et al²⁵ found revascularisation and incorporation of the grafts into a new trabecular structure without necrotic bone or significant remnants of the graft after 15 months. Similar histological patterns were found in specimens of femoral MBGs retrieved in revision THA.^{26,27} The revascularisation and remodelling potential

of MBG may be superior to that of the structural bone graft. Our results reflect the ideal biological situation when fresh autologous MBG is used for reconstruction. They should be interpreted with caution regarding the use of morsellised allograft since immunological factors may play a role in the incorporation process of bone grafts. Further experimental studies are required to determine the limitations of the application of MBG in larger femoral bone defects in revision TKA.

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