6 OVINE TUBE-STEM MODEL

6.1 Experimental methods

The ovine tube-stem model experiments were performed in close collaboration with Dr Ashley Blom, a surgeon from the Department of Orthopaedic Surgery at the University of Bristol. Thanks to his substantial support, the impaction grafting procedure could be performed according to the clinical protocols and a large number of samples could be tested.

The die-plunger compression test and the shear-box test provided information about the fundamental mechanical properties of bone grafting materials in response to compressive and shear loading in an idealised uni-axial environment. Although compression and shear are the dominant stresses on the bone graft in clinical impaction grafting, a correlation between the numerical characteristics derived from the standardised tests and a testing method which is more realistic, complex and clinically relevant must be established. Such an *in-vitro* model must be derived from graft preparation steps, the femur-stem geometry, loading regime and failure criteria in clinical impaction grafting while providing a high enough abstraction level of test geometry, sample preparation, loading scheme and test criteria to isolate graft properties as the major variable and to allow reproducible tests.

In this study two such models were developed: A human-scaled model described later in chapter 6 and an ovine-scaled model which was developed for ethical approval in preparation of an animal study in sheep described here. The human and the ovine models were used for graft impaction, implant fixation and subsequent endurance testing to failure.

The geometry of the ovine tube-stem model was designed to expose the graft reproducibly to a stress pattern comparable to that experienced *in-vivo*. Twenty sheep femora were measured to ascertain the inner dimensions of the proximal medullary canal. The morphology was found distally to resemble a cylindrical tube which widened slightly conically towards the proximal end with a mean diameter of 22mm derived from a 17-27mm range. Therefore aluminium tubes were constructed with an inner diameter of 22mm to mimic the geometry of the sheep femora. The slightly conical proximal cross-section was not modelled to allow the use of a single diameter distal impactor, a limitation required for experimental reproducibility.

The wall thickness of the aluminium tube resulted in a very stiff and strong model so that graft performance could be studied without the influence of variables such as the elasticity or strength of the medullary canal. In this way experimental reproducibility was improved further. A solid tube as a model which is stiffer than the ovine femur would increase graft stresses and could accelerate failure. This had advantages for both the ovine and the human model where it was the aim to develop a relevant but simplified model to identify relative comparisons in graft performance but not to derive numerical data which correlates directly to the clinical situation without conversion. The distal end of the tube had a thread to hold a distal plug which itself was threaded to screw in the guide wire. With the distal plug threaded into the tube the length of the medullary canal measured 100mm to allow proper stem insertion while maintaining sufficient distance between the distal end of the implant and the distal plug as advised in the surgical instructions. Figure 6.1 shows an illustration of the model and the experimental set-up.

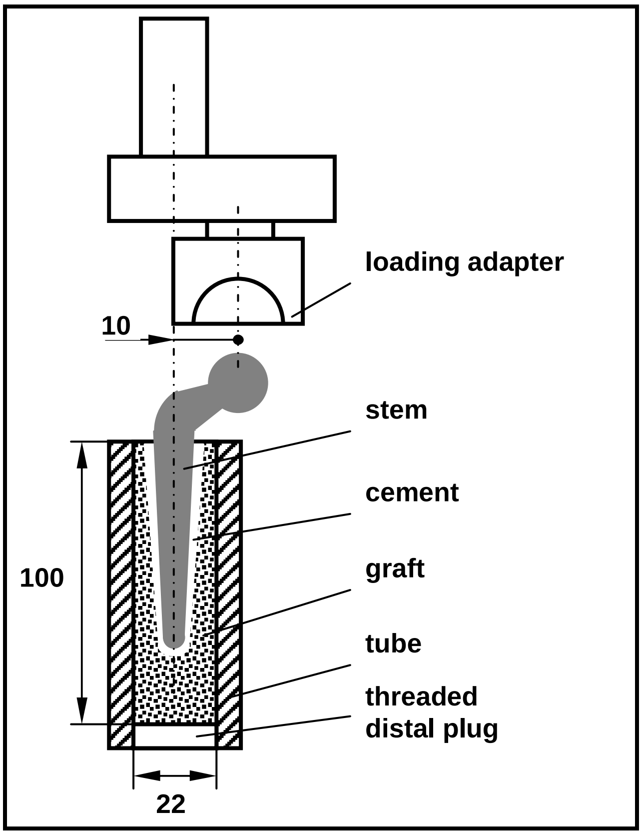

Figure 6.1:
Illustration of the ovine tube-stem model and the loading geometry.

The hip stems were not modelled but original, specially manufactured ovine hip stems from Howmedica, U.K were used. As in human impaction grafting, those implants were Exeter style, double tapered and polished hip stems with modular heads. Standard impaction grafting procedures were manually performed using an ovine impaction grafting tool kit specially designed by Howmedia, U.K. including guide wire, distal impactors and an oversized phantom prosthesis which was also used for proximal impaction. All samples were impacted vigorously with the distal impactors and the oversized phantom prosthesis until no further impaction was felt possible. At this stage the phantom could only be removed by with strong tapping and high pulling forces. The laboratory conditions allowed easy graft handling and model access and offered a solid support of the tube against a workbench so that impaction could be at least as vigorous as during the clinical impaction grafting when less convenient access and the lack of a solid support impede the impaction process. When sufficient graft was impacted as indicated by the position of the phantom prosthesis the femoral stem was cemented into the graft filled tube using standard clinical cementing techniques. The graft was sealed proximally with a cement layer. Samples were left to cure at room temperature for 24h.

Samples were then mounted in an Instron 8511 servo-hydraulic testing machine and cyclically block loaded in compression. Peak loads were derived from force plate measurements performed on thirty skeletally mature sheep giving peak ground reaction forces between 250N and 400N when walking. The loading regime consisted of 4 load blocks with 5000 haversine cycles each run at a frequency of 2Hz and a peak force increasing from 200N to 800N between load blocks separated by a 120s recovery period. A haversine wave format was preferred to a sine curve because it offers more step like loading gradients. The cycle frequency was chosen to simulate the gait speed of walking sheep and to guarantee that cement and graft materials could respond to loading with their viscoelastic damping properties *in-vivo*. Peak load, frequency and number of cycles correlate with the 1320N force cycled at a 1Hz frequency for 5000 cycles chosen to measure hip implant stability in another study on human cadaveric femurs[227].

The compression load was transmitted via an adjustable hemispherical polymer cup which allowed the cup to be individually aligned with the femoral head of the manually inserted prosthesis. The polymer cup was preloaded prior to experimental use in order to avoid plastic deformation during the cyclic loading interfering with the position readings and thus subsidence recordings. Reference measurements ensured that polymer creep at the high stress contact points between the metal ball and the cup during experimental loading stayed well below the resolution and error of the position signal. Due to the 10mm off-set of head and stem the load transfer direction was not vertically coaxial with the stem axis (figure 6.1) and introduced a bending moment into the cement and graft as experienced *in-vivo*. The set-up was designed to introduce no torsional moment. Vertical subsidence as a major failure mode in clinical impaction grafting[54] was recorded permanently by applying an averaging algorithm on the position signal acquired from the actuator LVDT using Hewlett-Packard DT-Vee software. The end point of each endurance test was defined as the completion of 20,000 load cycles or when a subsidence of greater than 5mm was measured. At this level the test geometry limited any further subsidence by contact between head or neck and the proximal tube. This corresponded to subsidence levels critical in ovine impaction grafting where resulting misalignment or contact between stem and femur could affect the gait or cause pain.

It was accepted for the experimental design that the modelled geometry and the simplified load transfer compromised direct quantitative comparisons of results with subsidence measured *in-vivo*. However graft materials were well isolated as the only major variable influencing stiffness and experimental reproducibility could be guaranteed. The ovine model tests were also conducted to better understand stability in impaction grafting in order to possibly allow the design of an improved human sized model. A summary of the experimental procedure is given as:

Design:

Femur: Stiff aluminium tube, cylindrical cavity: diameter d=22mm, length l=100mm

Stem: Ovine hip stem, Exeter-style, polished, double tapered, modular head

Load transfer: Vertical compression via hemispherical cup and femoral head, 10mm off-set

Sample preparation:

Grafting: Vigorous manual impaction grafting with Howmedica tool kit,

Stem fixation: Standard cementing technique, 24h curing at T_{Room}, proximal sealing

Mechanical testing:

Loading: Cyclic block loading in compression, haversine cycles, f= 2Hz, 5000 cycles per block, peak load per block: 200N, 400N, 600N, 800N

Data: Vertical subsidence s, failure criterion s> 5mm

6.2 Materials

The materials tested using the ovine tube-stem model were pure morsellised ovine bone graft and two graft mixes comprising ovine bone and granules of a synthetic ceramic bone graft extender. The ceramic extender was composed of 80% tri-calciumphosphate and 20% hydroxyapatite sintered at T_{Sint}= 1150°C and the 2-4mm granules contained a porosity of 50%. The ovine bone was morsellised using the Norwich bone mill and subsequently formalin fixed. The two graft blends had a mixing ratios of 1:1 bone/ceramic and 1:9 bone/ceramic by volume. Pure ceramic samples were not tested as the material lacked any cohesion and adhesion to be efficiently handled and packed thus appearing to be an inappropriate choice for testing. The small amounts of ovine bone added to the 1:9 bone/ceramic mix added sufficient cohesive and adhesive power to be handled and packed in surgery. Thus, the high ceramic content mix was defined as the opposite extreme to the pure bone samples. A summary of the materials tested follows:

- Pure ovine bone
- 1:1 bone/ceramic mix (20:80 HA/TCP, 50% porosity, T_{Sint}= 1150°C, *d*= 2-4mm)
- 1:9 bone/ceramic mix (20:80 HA/TCP, 50% porosity, T_{Sint}= 1150°C, *d*= 2-4mm)

6.3 Results

The impaction grafted and cemented ovine hip stem was cyclically block loaded in vertical compression and subsidence was recorded. The qualitative relationship between number of cycles or load blocks and the subsidence was identical for all samples, for all bone graft materials and for all load blocks tested. As can be seen in figure 6.2 cyclic loading initially caused very steep subsidence during the first ten cycles before establishing permanent subsidence with a logarithmically decreasing gradient. The gradient of the logarithmic function varied between load blocks and different materials. During the 2min recovery time between individual load blocks a significant fraction of the subsidence was recuperated by elastic recoil. Another qualitatively characteristic pattern with all materials and most samples was that the subsidence per load block increased with the rising peak load of the load block.

Comparing the relative stem subsidence of the different graft materials quantitatively identified ovine bone as the least stable graft and mixes of ovine bone with ceramic granules as the more stable grafts. This is shown in typical time-subsidence curves for the three different graft compositions (figure 6.2). The only stems which exceeded the failure criterion of 5mm subsidence before block loading was completed were amongst the group of samples impaction grafted with pure ovine bone. Four out of ten ovine graft samples failed prematurely before completion of the final 800N load block. Two of those samples even exceeded 5mm subsidence during the third load block at 600N peak compression force. All samples from both the 1:1 bone/ceramic (b/c) and the 1:9 b/c group of mixes survived without failure e.g. with less than 5mm subsidence after the final load block was completed after 20,000 cycles. The maximum subsidence recorded for all bone/ceramic mix samples was only 1.09mm.

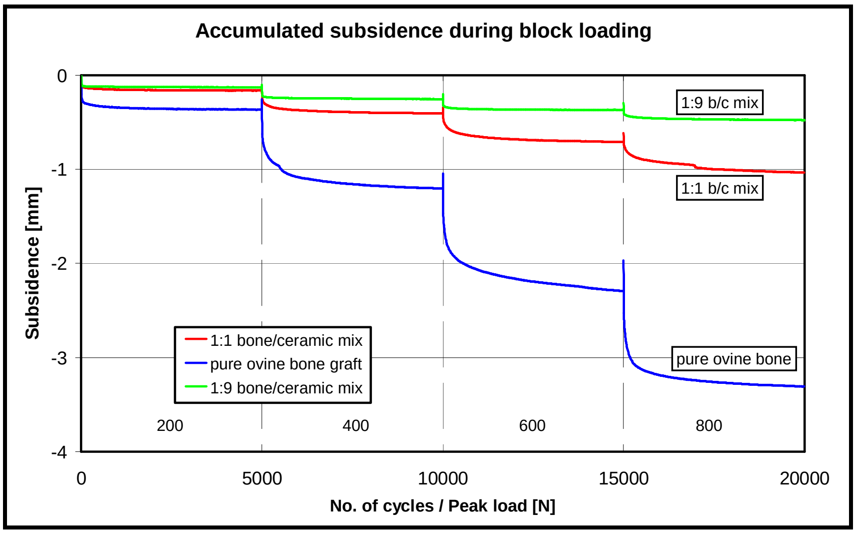

Figure 6.2: *Accumulated subsidence during cyclic block loading for typical samples of pure ovine bone and two bone/ceramic mixes with volume ratios of 1:1 b/c and 1:9 b/c.*

For more detailed numerical data analysis it was necessary to assign a subsidence value to bone samples which prematurely failed before completion of the final load block at 20,000 overall cycles. For those samples a maximum subsidence of 5mm equivalent to the failure criterion was assigned. A higher value seemed inappropriate and exclusion of those samples would have wrongly skewed the distribution towards higher stability. Table 6.1 summarises the stem subsidence measurements collected for all thirty samples.

	Pure ovine bone					1:1 bone/ceramic mix					1:9 bone/ceramic mix			
Peak load F [N]	200	400	600	800		200	400	600	800		200	400	600	800
Average Susidence [mm]	*0.43*	*1.82*	*2.87*	*3.83*		*0.14*	*0.27*	*0.40*	*0.54*		*0.11*	*0.19*	*0.27*	*0.36*
SD [mm]	0.36	1.68	1.72	1.49		0.07	0.12	0.18	0.24		0.08	0.10	0.11	0.13
SD [%]	83	92	60	39		52	45	44	45		73	52	40	37

Table 6.1: *Stem subsidence in the ovine tube-stem model for different graft compositions.*

Figure 6.3 illustrates the data in a bar chart and gives the average subsidence values measured after the completion of each 5000 cycles load block for the pure ovine bone and the two bone/ceramic graft mixes. Here the different stability levels of the various graft materials shown in figure 6.1 are validated by the numerical data derived from the statistical analysis of all 30 samples. Average subsidence of stems impaction grafted into pure ovine graft was the highest after each load block both in total and individually during each single load block. Both bone/ceramic mixes produced significantly less stem subsidence. Already during the initial load block with the lowest compression force stems impacted into pure ovine bone subsided by an average of 0.43mm. At the same time, average subsidence values recorded for the 1:1 b/c and the 1:9 b/c mix at 200N were only 0.14mm or 0.11mm respectively. This difference in stability increased towards higher loads so that after the completion of the final 800N load block, the average subsidence recorded for bone graft samples reached 3.83mm while the bone/ceramic mixes limited average stem subsidence to only 0.54mm (1:1 b/c mix) or 0.36mm (1:9 b/c mix). When an unpaired one-tailed student t-test was performed on the data all differences between the ovine bone graft and both the bone/ceramic mixes were statistically significant (1:1 mix versus ovine bone at 200N) or highly significant (table 6.2). In reality the lower stability of pure bone graft versus the bone/ceramic mixes would be even more pronounced. For numerical analysis, the four samples which failed prematurely were statistically registered with 5mm maximum subsidence at the end of a load block only. However it was also found that pure bone graft as the gold standard in impaction grafting can as well provide very high mechanical stability. One sample registered an accumulated total subsidence of only 0.41mm after the completion of the final load block, a value which was lower than 8 out of 10 samples of the, on average, more stable 1:1 bone/ceramic graft mixes.

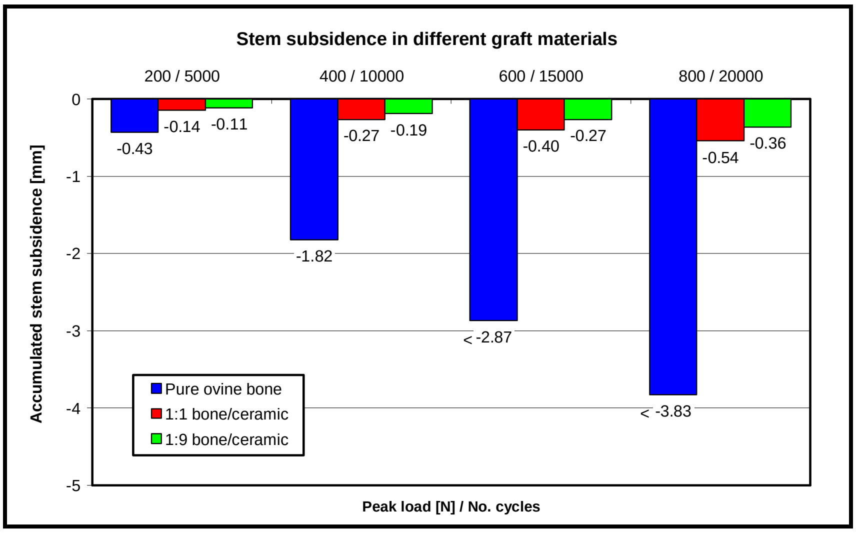

Figure 6.3:
Average accumulated stem subsidence during block loading of ovine bone and two bone/ceramic graft mixes at 1:1 and 1:9 volume ratio.

Such a potentially high stability and the low average stability with individual samples failing prematurely indicated that the mechanical performance of pure bone grafts is highly variable. This was confirmed by a comparison of the absolute and relative standard deviations calculated for the subsidence measurements listed in table 6.1 and graphically represented in figure 6.4. For the accumulated subsidence after each load block, the absolute standard deviation for ovine bone grafts samples was higher than for both bone/ceramic mixes ranging from 0.36mm to 1.49mm and 0.07mm to 0.24mm respectively. The same can be established for the relative standard deviation. The relative variation subsidence during the 200N and 400N load block is nearly twice as high for pure bone (83% and 92%) than it is for the 1:1 b/c mix (52% and 45%) or the 1:9 b/c mix (73% and 52%). The difference is probably even larger as absolute subsidence values for the ceramic graft mixes were so small that the measurements were more strongly affected by measuring tolerances and systematic errors increasing the standard deviations.

Statistical Analysis: Unpaired one-tailed student t-test				
	p-values			
Load block / Comparison	*200N*	*400N*	*600N*	*800N*
1:1 bone/ceramic mix vs pure ovine **bone**	<0.025	<0.010	<0.005	<0.005
1:9 bone/ceramic mix vs pure ovine **bone**	<0.005	<0.005	<0.005	<0.005
1:9 bone/ceramic mix vs **1:1** bone/ceramic mix	n.s.	n.s.	<0.05	<0.05

Table 6.2:
Statistical significance levels for comparisons of stem subsidence between different graft materials using the unpaired one-tailed student t-tests

As adding ceramic granules to a pure bone graft increased stability against subsidence, raising the ceramic volume fraction in such a graft mix did further increase stability (figure 6.2 and 6.3). After completion of the loading regime after 20,000 cycles, stems impacted into a 1:1 b/c graft mix had subsided on average by 0.54mm while for the 1:9 b/c samples only 0.36mm subsidence was recorded. Although average subsidence was higher and thus stability lower for the 1:1 than for the 1:9 b/c mix after all load blocks, the differences were only statistically significant at the higher 600N and 800N peak forces (table 6.2). The standard deviations for the subsidence measurements after the 400N, 600N and 800N load blocks were lower for the high ceramic content mix than for the 1:1 b/c mix indicating an improved reproducibility of graft stability when the ceramic fraction is raised (figure 6.4). However, in relative terms, standard deviations for the 1:1 and the 1:9 b/c mix are too similar to confirm this trend. Low subsidence values and comparatively high measuring tolerances and errors might disguise a potentially significant trend.

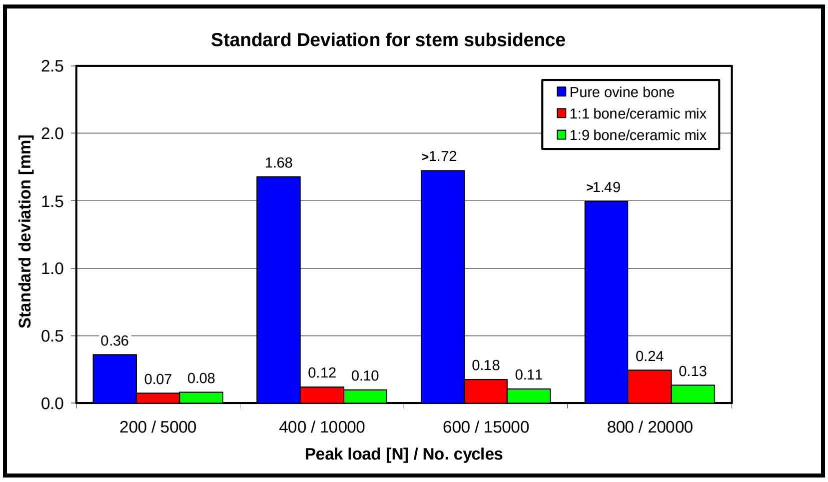

Figure 6.4:
Standard deviations of stem subsidence measurements for different graft materials after completion of different load blocks.

So far graft stability has been expressed as the accumulated subsidence measured after the completion of each load block. When subsidence accumulated during each individual load block is represented as a funtion against a logarithmic axis for the number of cycles, straight trendlines with characteristic slopes can be produced as shown in figure 6.5 for representative samples of pure ovine bone, 1:1 and 1:9 b/c graft mixes. As can be seen, for all graft materials and peak loads, subsidence increased logarithmically with the number of cycles. The logarithmic trendlines calculated and plotted against a logarithmic axis for the number of cycles produced straight lines with R^2-values ranging between 0.942 and 0.992 (average 0.973) indicating good agreement with the mathematical assumption.

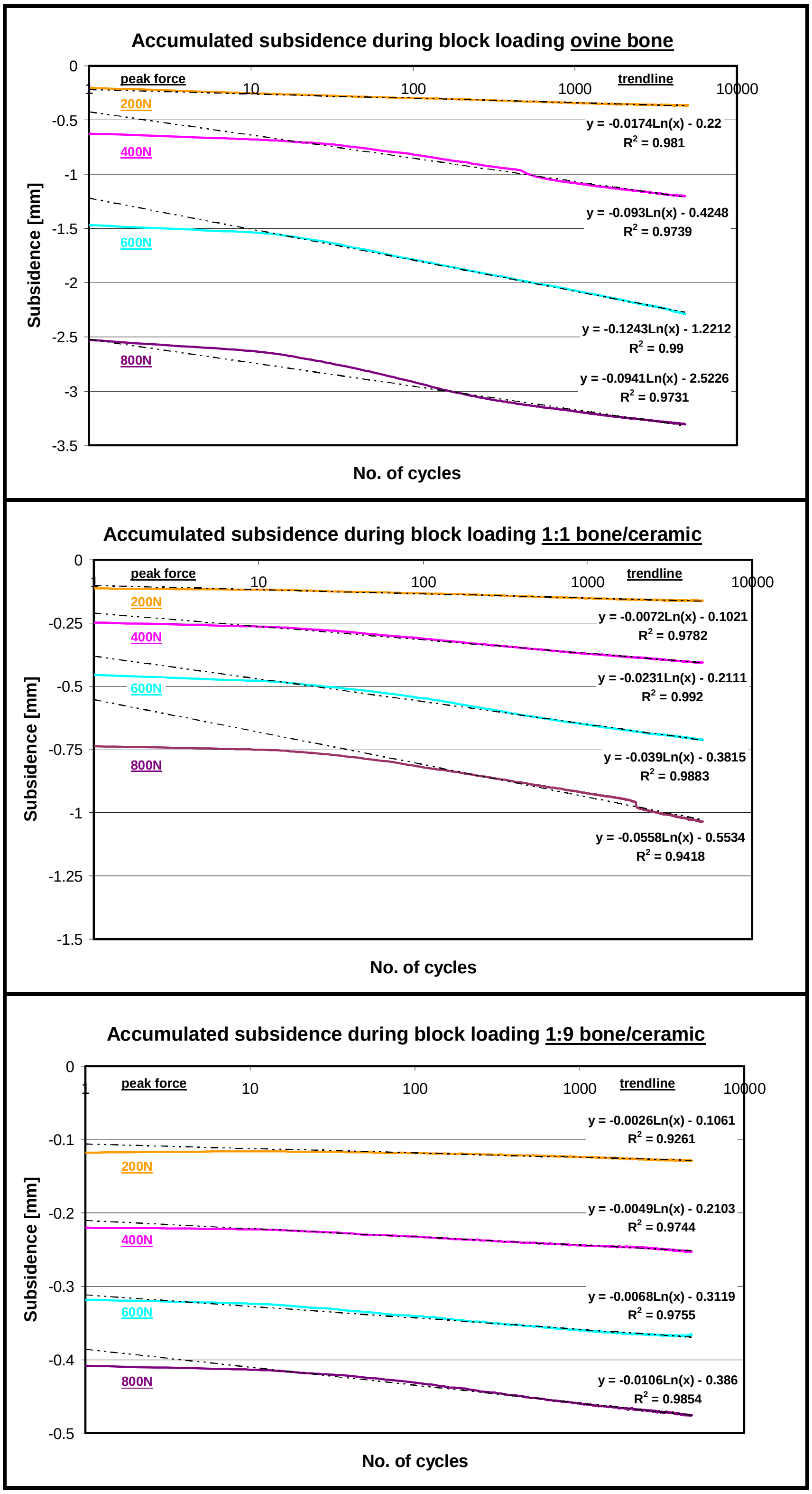

Figure 6.5: *Accumulated stem subsidence during block loading of an ovine bone sample (top), a 1:1 (centre) and a 1:9 bone/ ceramic mix (bottom).*

The subsidence curves represented in figure 6.5 exclude the first data point and thus the vertical displacement produced during compression loading for the first one to ten cycles. Figure 6.6 represents the subsidence curves for pure ovine bone and the 1:1 bone/ceramic mix when these data points are included and it can be seen that the logarithmic relationship between accumulated subsidence and number of cycles only established itself after an initial sink in period during the first few load cycles. Only after ca. 10 cycles the subsidence curves followed the logarithmic trendlines in good approximation.

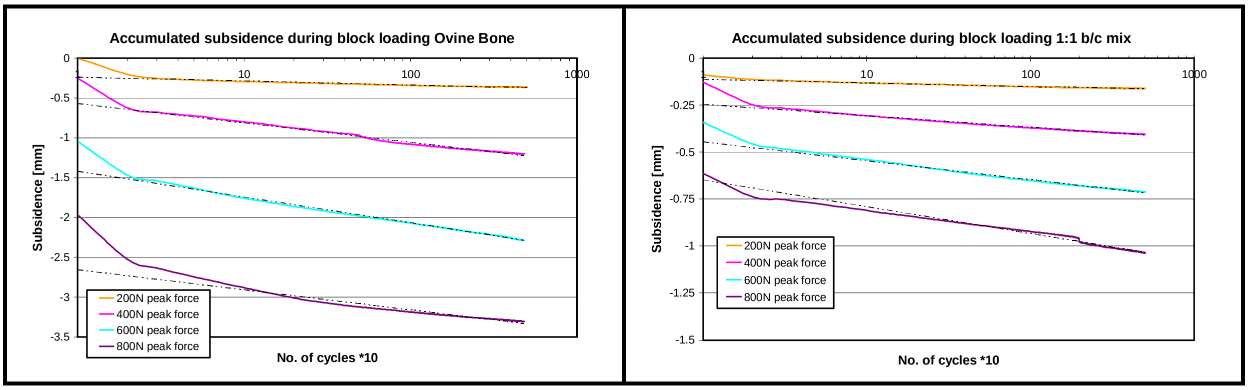

Figure 6.6: *Accumulated stem subsidence during block loading of an ovine bone (left) and a 1:1 b/c mix sample (right). The number of cycles are represented on a logarithmic scale.*

Referring back to the subsidence curves represented in figure 6.5, a clear correlation between the graft materials or peak loads and the logarithmic subsidence rates can be identified. Figure 6.7 highlights this relationship by superimposing the logarithmic trendlines from figure 6.5 into one graph to simplify comparison against a constant axis for subsidence. Comparing the graft stability at one peak load shows that the subsidence rate was the highest for the pure bone graft sample and the lowest for the high ceramic content 1:9 b/c mix. The equally blended 1:1 b/c lay in-between. When the peak force was increased the subsidence rates increased for all samples and between all load blocks except between the second last (600N peak force) and the final load block (800N) of the pure bone graft sample.

Figure 6.8 numerically represents the subsidence rates α as calculated in equation 6.1 and measured in micrometer subsidence per natural logarithm of the number of cycles N:

$$s = -\alpha * \ln N - c \qquad \textit{(equ. 6.1)}$$

s= accumulated subsidence
α= subsidence rate, $[\alpha]= \mu m/\ln N$
N= number of cycles into load block
c=vertical start position

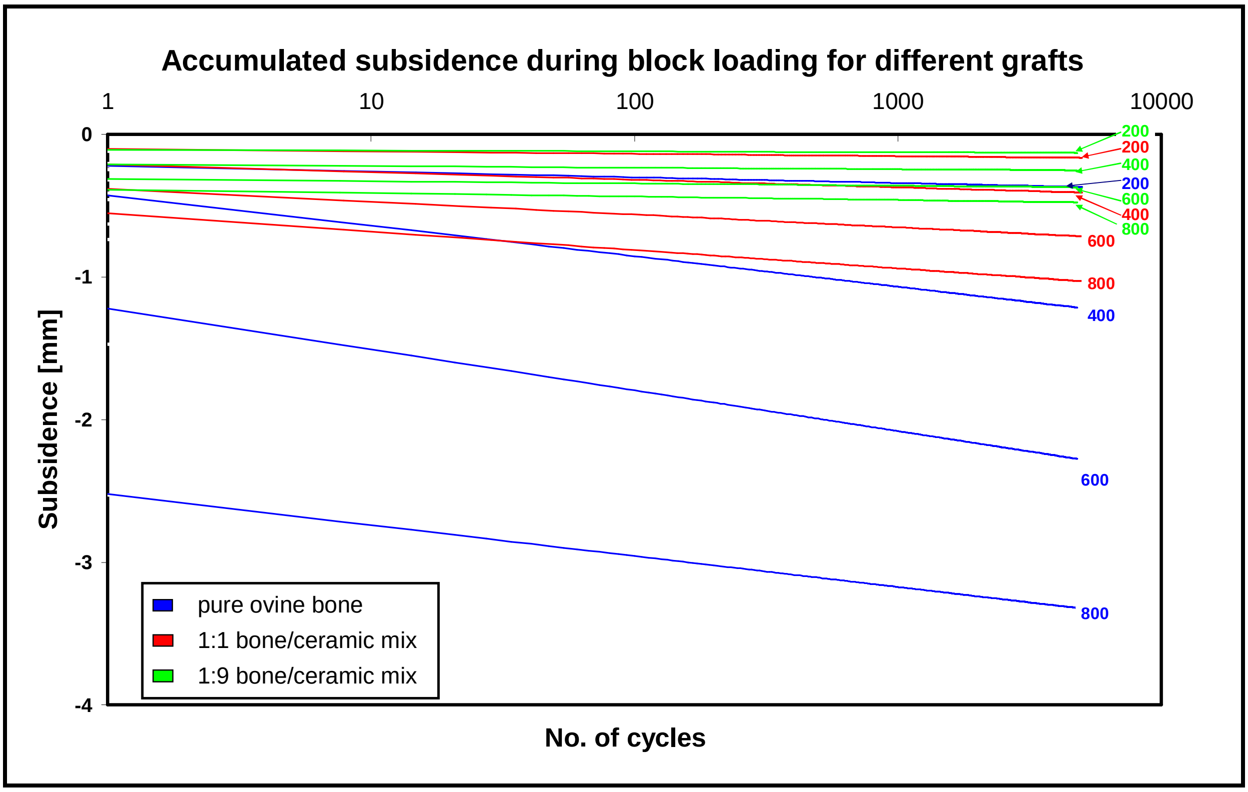

Figure 6.7: *Logarithmic trendlines of subsidence accumulated during cyclic block loading superimposed for typical samples of pure ovine bone, a 1:1 and a 1:9 b/c graft mix.*

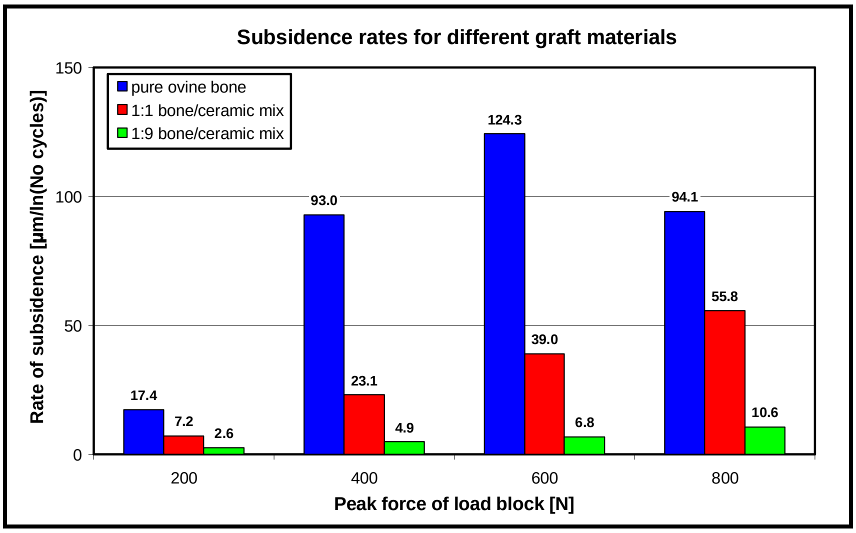

Figure 6.8: *Average accumulated stem subsidence during block loading of ovine bone and two bone/ceramic graft mixes at 1:1 and 1:9 volume ratio.*

Already at the lowest 200N peak load when subsidence rates are very low and total subsidence is minimal, the different subsidence rates clearly distinguish the stability performance of different graft materials. During the 200N load block, pure ovine bone graft produced the highest subsidence rate measuring a= 17.4 µm/lnN while the 1:1 b/c graft mix only subsided at a rate of a= 7.2 µm/lnN. For the high ceramic ratio 1:9 b/c mix a subsidence rate of only a= 2.8 µm/lnN was calculated. For pure bone and both graft mixes the subsidence rates increased when the peak load was increased except for the final 600N to 800N peak force rise of the pure bone graft sample.

Comparing both graft mixes, a higher subsidence rate also lead to an absolutely higher increase in subsidence rate when the peak forces were increased as shown in table 6.3. This resulted in highly accelerated vertical displacement towards the failure position for graft mixes less stable at low peak forces. The subsidence rate of the stem impacted into a 1:9 b/c mix increased from *a*= 2.6 μm/lnN during the 200N load block to finally 10.6 μm/lnN during the 800N load block, a change of 308%. The 1:1 b/c mix produced an average subsidence rate of *a*= 7.2 μm/lnN during the 200N load block showing its inferior stability at the lowest load level already. During the final 800N load block, its subsidence rate measured *a*= 55.8 μm/lnN, an increase of 675%. The same observation can be made for the pure bone graft between the 200N and the 400N and between the 400N and 600N load block.

Peak force	Graft	pure bone	1:1 b/c mix	1:9 b/c mix
200N load block	**Subsidence rate [μm/lnN]**	**17.4**	**7.2**	**2.6**
400N load block	**Subsidence rate [μm/lnN]**	**93**	**23.1**	**4.9**
	Abs. increase [μm/lnN]	+75.6	+15.9	+2.3
	Rel. increase [%]	*+434.5*	*+220.8*	*+88.5*
600N load block	**Subsidence rate [μm/lnN]**	**124.3**	**39**	**6.8**
	Abs. increase [μm/lnN]	+31.3	15.9	1.9
	Rel. increase [%]	*+33.7*	*68.8*	*38.8*
800N load block	**Subsidence rate [μm/lnN]**	**94.1**	**55.8**	**10.6**
	Abs. increase [μm/lnN]	-30.2	+16.8	+3.8
	Rel. increase [%]	*-24.3*	*+43.1*	*+55.9*

Table 6.3: *Stem subsidence rates for different graft materials after during different load blocks.*

Impaction grafting with the ovine model also revealed important qualitative observations. Ovine stems retrieved after testing showed uneven cement mantle thickness confirming a clinically observed problem in even the idealised experimental environment where a symmetrical canal geometry, good access and easy handling simplify the procedure. When the samples were retrieved the stems could be pulled out of the impacted graft with the cement mantles still strongly attached to them. The outer cement mantle surface was rough and clearly visible through a thin layer of sprinkled individual bone graft particles attached to it. It became clear that the interface strength between the stem and the cement is much higher than between the cement and the graft. The depth of cement penetration into the porous graft was low in comparison to the dimensions of the graft particles. No intermediate composite layer was formed resembling a bone particle reinforced cement matrix. The results from endurance testing with the ovine model are summarised in table 6.4.

During cyclic loading of an impaction grafted stem:
• Subsidence was very steep during the first cycles.
• After the initial phase, subsidence increased logarithmically with the number of cycles. subsidence = f (lnN)
• The stability of bone/ceramic graft mixes was significantly higher than for pure bone: Stability 1:1 b/c mix > bone, stability 1:9 bc mix > bone
• A higher ceramic content in the bone/ceramic mix increased stability significantly: Stability 1:9 b/c mix > 1:1 b/c mix
• Pure bone graft can provide high stability but often collapses prematurely and suddenly.
• The subsidence rates **α** were a function of graft material and peak load. **α** = f (material, peak load)
• The higher the subsidence rates at low loads the higher their increase towards higher loads. ⇒ accelerated failure
• Stability variations were lower for both bone/ceramic graft mixes than for pure bone. $SD_{bone} > SD_{bone/ceramic\ mix}$
• Stability variations between both bone/ceramic graft mixes were similar. $SD_{1:1\ mix} \approx SD_{1:9\ mix}$

Table 6.4: *Summary of conclusion drawn from endurance testing with the ovine model.*

6.4 Discussion

- **General**

Prior to the discussion of the observations relevant to the clinical application of impaction grafting two important aspects of the experiment should be recalled. Firstly, *in-vitro* tests of impaction grafting can naturally only assess the initial stability of the graft composite. Graft stability in the long term is influenced by biological factors *in-vivo* such as revascularisation and osteogenic activity which cannot be replicated in *in-vitro* experiments. However, according to the literature, significant and functionally critical subsidence leading to failure *in-vivo* most often occurred within three months post-operatively, a time period where no stabilising bone remodelling can take place[29]. Thus the limitation of the *in-vitro* experiments to assess the initial stability alone seems highly appropriate.

A second aspect to be recalled is that a large range of factors affect the subsidence of allografts *in-vivo* and that an *in-vitro* laboratory experiment must focus on selected variables while keeping the remaining factors constant. Such factors include graft preparation and quality, particle morphology and size, graft composition, impaction techniques, cementing techniques, morphology and condition of the femur, condition and health of the patient, the host's immune response and the host/ graft interface or post-operative loading. The ovine sized impaction grafting model focused on the influence of graft composition on stability by isolating the intrinsic mechanical graft properties as the only variable.

- **Discussion of qualitative results**

Qualitatively, subsidence accumulated in the same way for pure bone, a bone plus ceramic graft mix of equal volumes and the graft composition with a dominant fraction of ceramic. In all samples vertical displacement started with a steep drop during the first few cycles of each load block and was followed by a slow exponential subsidence with a constant logarithmic rate. Qualitatively identical and quantitatively similar observations are reported in a study on implant stability in impaction grafted human cadaveric femurs[227]. This confirms the validity of the experimental model.

Qualitatively identical subsidence for pure bone grafts and both ceramic/graft mixes at any peak load suggests that the subsidence mechanisms at work are the same independent of graft material and compression force. The steep subsidence during the first approximately 10 cycles was the combined result of elastic and thus recoverable deformation plus a further degree of irrecoverable graft compaction introduced by the first load cycles in a similar way as a set of additional hammer blows. The initial drop was the highest for bone as the least stable graft with the highest subsidence rate and the lowest for the 1:9 b/c mix which was the most stable graft. The initial drop increased with the peak force of each load block but the ratio between elastic and plastic deformation was variable. However, no significant differences between the graft materials or peak force could be identified further confirming the hypothesis of identical subsidence mechanisms at work independent of material or load. Cement elasticity contributes to the elastic recovery after unloading and might dominate the recoil effects of different grafts with different visco-elastoplastic properties.

- **Discussion of quantitative results**

Graft stability was quantified as the total subsidence accumulated during cyclic loading and by the constant logarithmic subsidence rates. With regards to both assessments the graft mixes containing fractions of the synthetic bone graft extender achieved higher and less variable stability than pure bone grafts. A higher ceramic fraction in the graft mixes significantly improved stability further. Individual bone graft samples achieved equally high stability as the graft mixes but the majority failed prematurely. These observations confirmed results and interpretations drawn from the die-plunger and shear-box experiments. Here, pure bone grafts showed weaker compression moduli and shear strength than the ceramic materials so that bone/ceramic mixes had mechanically superior properties which improved when the volume fraction of the ceramic phase was increased. The improved mechanical performance of the graft mixes versus the pure bone was evident during die-plunger testing even at low loads and this observation was found also for the stability against subsidence under cyclic loading of the ovine stem-tube model. All major differences in graft stability at the maximum peak load and after significant subsidence were obvious even during cycling at the lowest peak load. Relative differences in graft performance at low loads increased towards higher loads. Thus the mechanisms of stem subsidence into an impacted and geometrically constrained graft must be fundamentally independent of material and load. As this mechanism leads to constant logarithmic subsidence rates for all materials and peak loads tested, ultimate stability in the sense of zero subsidence for a specific graft or loading situation cannot be achieved. Subsidence can only be limited to a rate below a tolerable threshold.

The relative increase of subsidence rates towards higher loads slowed down and even reversed for some samples where the accumulated subsidence reached values close to the failure criterion of 5mm vertical displacement, a dimension chosen in analogy to subsidence levels clinically considered as failures. It was also a geometrical limit of the experimental design. This behaviour which seems like a graft stabilising effect is the consequence of graft displacement inhibited by proximal sealing of the femoral cavity. During subsidence of the tapered stem into the tube modelling the femoral cavity, the stem requires an increasing proportion of the available cylindrical (experiment) or conical (*in-vivo*) space. If the graft is proximally sealed, the subsiding stem cannot make space for itself by proximal displacement of graft but only by compressing the graft further or by deformation of the constraining volume, e.g. by expansion of the femoral cavity or displacement of the distal plug. As the dense cortical bone of the femoral canal *in-vivo* or a solid aluminium tube *in-vitro* will not deflect sufficiently to create additional space, the compactable bone graft is condensed further when the stem subsides. Such additional compaction increases the graft stability in a similar way as intense impaction prior to stem insertion. In addition any material will ultimately become extremely stiff when compressed into a solid mould providing geometrical constraints in all dimensions similar to the die-plunger compression test where this effect was observed as well. Thus, when the stem had subsided by several millimetres into a tube well sealed proximally by cement, the subsidence rates could decrease again.

The relative graft performance between pure bone and bone/ceramic mixes was the same during standardised die-plunger compression testing of loosely packed graft and during endurance testing of a femur-stem model where intense manual graft impaction preceded the loading regime. Such hard hammer blows are expected to exceed peak forces of a few thousand Newtons for very short times and they break up significant fractions of the highly friable ceramic phase in the bone/ceramic mixes. The effect must be particularly strong for graft mixes containing a high ratio of ceramic with little bone graft and its viscoelastic organic tissue softening the load transfer into the graft or reducing direct contact points between individual ceramic granules which act as stress risers. However, despite this effect of particle fracture and dusting which was also observed during experimental impaction, the mechanical superiority measured for graft mixes containing ceramic granules during the die-plunger compression tests prevailed during cyclic testing of heavily compacted and thus fractured or pre-damaged grafts. The stability of the fractured granules must still be sufficient to raise the stability of the graft mix. In addition ceramic fracture during impaction might alter the overall particle size distribution in a mechanically favourable way so that denser graft packing is possible which compensates for the ceramic particles fragmented to dust.

As expected, another observation made during the die-plunger compression tests was confirmed during fatigue cycling the graft in the stem-tube model as well. The stability variations calculated as standard deviations of the subsidence levels measured for different graft materials were higher for pure bone graft than for both graft mixes containing either 50% or 90% ceramic granules. The standard deviations between both b/c mixes were similar so that increasing the ceramic content above 50% did significantly enhance stability but not further reduce variability. The less variable mechanical performance of bone graft mixes is the result of the stable and easily controllable parameters such as chemical composition, sintering conditions or particle size of the ceramic phase versus the naturally variable properties of bone. This reduction in variability was statistically significant despite using a bone graft of maximised consistency. Ovine xenograft sourced from equally sized and aged sheep was morsellised at once and mixed into large batches to level out inconsistencies.

6.5 Conclusions

- **Model validation**

Conclusions from the ovine sized tube-stem model can be drawn with reference to the experimental procedure and to implications for the clinical application of impaction grafting. Considering the experimental design and procedure it can be concluded that testing impaction grafting with the ovine tube-stem model is a valid experimental abstraction with clinical relevance. It produces qualitatively identical and quantitatively similar subsidence as reported in an implant stability study on human cadaveric femurs[227]. Also, using the model, pure bone graft revealed characteristic properties reported from clinical studies. Both in clinical application and in the experiments impaction grafting with bone graft was able to provide high stability but also frequently failed with sudden and massive subsidence. It seems that the experimental design and *in-vitro* procedures are valid simplifications to analyse the initial mechanical stability of impaction grafting and derive clinically applicable results. In particular modelling the complex shape of femoral canal with a solid tube featuring a cylindrical cavity and limiting both loading and subsidence control to the vertical direction only can be accepted as sensible abstractions when testing of impaction grafting is designed to isolate the graft properties as the major variable.

Loading the stem and graft in blocks of increasing peak force proved to be essential to allow the detailed analysis of the subsidence behaviour of materials with widely different stability levels. An alternative loading regime cycling at one constant peak force until failure only would provide less information about the graft materials. Critical loads leading to sudden and massive subsidence as observed for the bone grafts could be missed. Cycling at one peak load until failure only could also result in experiments which, when the load is too low, are either excessively long, not revealing the critical failure modes of a graft material at all, or, when the load is too high, are either too short to resolve the stability performance and failure modes. This concern is especially valid when a test procedure is supposed to analyse an array of graft materials or variables of the impaction grafting procedure with an even wider range of properties. Additionally, for all load blocks the subsidence rate quickly settled at a constant logarithmic rate after only a small number of cycles allowing early prediction of further subsidence and ultimately failure. Therefore a continuation of cycling to failure at this one peak load does not provide additional information.

The only argument in favour of testing at just one peak force is that relative differences in graft stability measured at any one peak load remained the same at all other loads, even when this one peak load was low and thus subsidence very small at values which are clinically not critical. With this information in mind it would be possible to define a highly simplified and accelerated loading regime for testing the stability of impaction grafted materials. Only one peak load is applied and cycling stops as soon as the logarithmic subsidence has clearly established itself. The cyclic loading could be terminated when enough data points are collected to derive a subsidence rate with a certain R^2-value representing the accuracy of the interpolation. For the graft materials tested using the ovine sized tube-stem model R^2-values of more than 0.95 were reached already before the completion of 100 cycles. The derivation of a characteristic subsidence rate for a graft material would be possible after less than 1min of cycling. Block loading or cycling to failure can take several hours or days.

- **Clinical implications**

Diverse implications for the clinical application of impaction grafting can also be derived from the ovine tube-stem model. Clinical impaction grafting using morsellised bone can provide very high mechanical stability and in combination with its osteogenic properties has rightly established itself as the gold standard material. The wide divergence of stability levels clinically observed in impaction grafting is mostly attributed to insufficient compaction levels or surgeons not experienced enough with the procedure. In the experimental situation graft compaction was very intense and much more reproducible than in the operating theatre. The geometry of the cavity, access to it, handling of the tools and a solid surface to compact against made the procedure much more easy. Nevertheless, the wide stability divergence was observed in the laboratory tests as well identifying the bone graft as a major reason for the highly variable clinical success rates. In the experiment b/c mixes lead to significantly reduced variability supporting the assumption that the experimental procedure can be excluded as the major source of inconsistencies. In clinical impaction grafting the variability introduced by the morsellised bone graft must be expected to be even larger than in the experiment because the variability inherent in the one to three human femoral heads commonly used for one operation is higher than in a mixture of a ten to twenty humeral heads from equally sized healthy sheep. As variability was even high for the relatively consistent ovine graft it cannot only be the result of inconsistent properties between individual femoral or humeral heads but it must lie in the nature of the material itself. With morsellised bone graft not being one homogenous but a multiphase material consisting of cancellous particles, cortical fragments, various types of soft tissue plus various fluids like blood, the preparation of a homogenous bone graft matrix within the femoral cavity seems impossible. One can speculate that pre-operative washing of the graft which has been reported to improve clinical results[224] might be the consequence of reducing graft variability by washing away blood and soft tissue so that a more dominant bone mineral fraction provides more consistency.

Regardless of the mechanical stability provided, all graft materials during all load blocks showed qualitatively the same subsidence behaviour, an initial steep drop followed by exponentially decreasing subsidence. For clinical application this means that for any graft materials used and regardless of the impaction intensity delivered, ultimate initial stability seems unattainable. A combination of relatively high initial elastic plus irrecoverable deformation will be followed by permanent subsidence at a constant logarithmic rate. In theory, any graft material would ultimately lead to stem subsidence beyond the failure position if cycled for long enough. Only graft incorporation and bone remodelling which converts the graft from a particulate aggregate into a solid bone mass connected to the skeleton could stop this process and provide long-term stability. Alternatively, the impacted graft must be so stable that the subsidence rate is so low that no clinically critical subsidence accumulates over the life-time of the patient or prosthesis. However, for initial stability, a tolerable level of such subsidence must be considered and accepted in impaction grafting.

A maximum tolerable subsidence rate for the phase of initial mechanical stability between surgery and bone remodelling could be estimated when assumptions are made for the duration of the remodelling process, a clinically acceptable total subsidence during this period and the loading intensity and frequency of the patient. If the data base from the ovine model could be increased by more tests, a map of subsidence rates, peak forces, graft materials and other impaction grafting variables could be produced. A transfer between experimentally derived and clinically tolerable subsidence rates seems possible. However, two potentially critical effects remain unconsidered, the micromotion levels (graft stiffness) tolerable for graft revascularisation and subsequent incorporation and the potential drop in mechanical stability during this process.

A major conclusion from the ovine tube-stem experiments with high clinical relevance is that adding ceramic granules of the tested configuration (80:20 HA/TCP composite, 50% porosity, T_{Sint}= 1150°C, 2-4mm granule size) into a bone/ceramic graft mix promises to significantly improve stability and reduce variability in impaction grafting over pure bone. The increase in stability was so large and statistically so significant for the 1:1 bone/ceramic mix already that its clinical application can safely be recommended.

Increasing the ceramic content further up to a level where the bone graft only acts as a filler providing some cohesion improved stability even more. The highly reduced variability calculated already for the 1:1 b/c mix was maintained for the 1:9 b/c mix. Thus even high ceramic admixtures are clinically superior to pure bone graft. The correlation between increased ceramic content and increased stability plus the improved variability of all graft mixes ensures that adapting the bone/ceramic mixing ratios to clinical indications, the surgical preferences or for scientific purposes will not negatively affect the stability but will always be superior to the gold standard bone. Using ceramic granules as a synthetic bone graft extender introduces another surgical step into an already complex procedure prone to subjective judgement, personal experience and potential error. However such a persistent improvement of stability and variability provided by the ceramic independently of the mixing ratio, promises safe application even if surgeons deviate from recommended mixing ratios by error or if ensuring a homogenous distribution of granules in the femoral canal cannot be achieved.

The friable nature of the ceramic granules which results in particle fracture and dust production under heavy impaction required for optimum stability proved not to be problematic with regards to stability. The 1:9 b/c mix did produce most particle fractures and the highest level of dust production but still delivered the highest stability. This observation can lead to the conclusion that the particle size of the ceramic granules is not such a critical parameter if the particles are small enough to allow proper mixing and charging. The relatively weak influence of ceramic particle size on the mechanical performance of a compressed particulate aggregate was already shown in the die-plunger tests and confirms this conclusion.

Although higher ceramic contents in graft mixes increase stability further, biological aspects must be taken into consideration when an optimal mixing ratio is to be derived for clinical application. As qualitatively observed during testing, mixes rich in ceramic produce more dust under heavy impaction than mixes with equal volumes of bone and synthetic extender. When the ceramic fraction is dominant more HA/TCP granules are in direct contact with each other and less soft tissue is present to dampen the hammer blows and to create a smooth load transfer into the graft with less stress concentrations. The result is multiple particle fractures; such dust particles can reach cytotoxic dimensions which could cause aseptic loosening in the same way as wear particles from the articulating surfaces of a hip replacement, a major cause for premature failure in primary hips. Considering in addition the importance of graft incorporation and bone remodelling for long term stability and assuming that bone graft provides osteogenic potential superior to any synthetic extender, limiting the ceramic content in a bone/ceramic mix to a 1:2 volume ratio seems sensible. A significant increase in stability can be achieved while maintaining significant osteogenic potential and limiting the risk of excessive production of cytotoxic dust particles. This way biological and mechanical requirements can be balanced. A summary of conclusions is given in table 6.5.

- **Stem subsidence qualitatively identical between ovine model and a study on human femurs**
  ⇒ Model validation
- **Bone grafts can provide stability but can also fail early with massive subsidence**
  = Identical observations with model and *in-vivo* ⇒ model validation
- **Block loading required to allow detailed analysis of a wide range of graft properties**
- **Exponential subsidence with constant logarithmic rate established after a few load cycles**
  ⇒ Short test series possible
  ⇒ Subsidence is permanent
    → Subsidence can only be kept below tolerable level
    → Some initial subsidence must be accepted
    → Only bone remodelling can lead to total long term stability
    → Proximal graft sealing can reduce subsidence rate
- **Adding HA/TCP granules into a bone/ceramic mix**
  ⇒ Higher stability, lower variability → Recommendation for HA/TCP granules as a bone graft extender
- **Increasing ceramic fraction in graft mix** ⇒ stability improved further, low variability remains
    → Substituting more bone graft is mechanically beneficial
    → Varied mixing ratios are clinically not critical
- **Ceramic particle crushing and dusting under vigorous impaction**
  ⇒ Stability advantage is maintained → Original ceramic particle size less critical
  ⇒ Ceramic dust = Particles of cytotoxic dimensions → Risk of osteolysis
- **High ceramic fraction**
  = increased mechanical stability
  = more potentially cytotoxic particles
  = less bone graft with osteogenic potential
  ⇒ Optimum b/c mixing ratio = compromise between mechanical and biological requirements

Table 6.5: *Summary of conclusion drawn from endurance testing with the ovine model.*