Time-Dependent Mechanical Properties of HA/TCP Particles in Relation to Morsellized Bone Grafts for Use in Impaction Grafting

Orthopaedic Research Laboratory, University Medical Center Nijmegen, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands

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Abstract: In reconstructive surgery human bone defects are sometimes filled with the use of the impaction bone grafting technique. Currently different types of biomaterial particles are being developed as bone-substitute materials. Before these biomaterials can be applied their mechanical and biological behavior should be characterized. In this study the time-dependent mechanical behavior of biomaterial particles with different tri-calcium-phosphate/hydroxyapatite (TCP:HA) ratios, particle sizes, and porosities is determined and compared to the behavior of human bone grafts, the latter being the standard material currently used to augment bone defects. The mechanical properties were assessed with the use of dynamic confined compression creep tests with a loading and unloading phase. Different graft material groups were tested, consisting of 100% human bone grafts, 100% biomaterial particles, and 50:50 weight mixtures of human grafts and biomaterial particles. No damage to the particles was observed by the impaction in the test chamber or by the dynamic load. Relative to the human graft material, the biomaterial particles hardly deformed under loading, were much stiffer, and showed almost no viscoelastic behavior. The mixtures showed intermediate results. Particle size and porosity influenced the behavior of the biomaterial particles. TCP:HA ratio did not have a great effect. The conclusion is that the application of these particles should be done with great care, as their mechanical behavior is drastically different than that of the human graft material. Mixing it with human bone grafts gave the material some biphasic, viscoelastic behavior that may be important for its biological response. © 2001 John Wiley & Sons, Inc. J Biomed Mater Res (Appl Biomater) 58: 599–604, 2001

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INTRODUCTION

The loosening process of failed total hip prostheses and the procedures to remove the prosthesis and the cement during revision induce bone destruction, resulting in widening of the femoral shaft and defects in the acetabulum. Morsellized human bone grafts can be used to fill bone defects in revision surgery and reconstructive surgery. The long-term success rates with this technique on the acetabular side and the femoral side are excellent. In spite of these good results with human morsellized bone grafts, the clinical results are considered to be highly technique dependent. In addition, human allograft material is available in limited volumes and there is a risk of transmitting infections. For these reasons, synthetic bone substitutes or synthesized xenografts are being developed to serve as bone-substitute materials.

Good alternatives for human bone grafts may be synthetic biomaterials like tricalciumphosphate (TCP) and hydroxyapatite (HA). Moore, Chapman, and Manske tested three groups of graft materials in bridging large diaphyseal defects in the canine ulna. These three groups consisted of 100% morsellized TCP:HA, 100% autogenous bone grafts, and a 50:50 mixture of morsellized TCP:HA with autogenous bone grafts. This study showed that a morsellized ceramic consisting of TCP and HA, when mixed in a 50:50 ratio with autogenous bone grafts, is biocompatible, capable of providing a matrix or scaffold for the ingrowth of bone, and comparable with autogenous bone grafts in filling defects.

Synthetic substitutes like TCP and HA are attractive because they are readily available and easy to use during surgery. TCP/HA composite biomaterials are available with different TCP/HA ratios, porosities, and particle sizes. These parameters may have an effect on the mechanical and biological response of the biomaterial. It is important to know what the response to a dynamic mechanical load of these particles is before they are used clinically. Do the particles crunch under impaction or under subsequent dynamic load, or do they slide relative to each other, thereby jeopardizing the integrity of the reconstruction? Do they deform elastically to a considerable level and show a viscoelastic behavior result-
ing in a pumping mechanism of fluids and blood around and in the graft? What are the effects of TCP/HA ratios, porosities, and particle sizes of the particles on these properties, and how do they change if the particles are mixed with human bone grafts?

To answer these questions the mechanical behavior was characterized by three parameters: The time-dependent deformational behavior, the stiffness, and the viscoelasticity of the materials. The method used to test the time-dependent mechanical properties in vitro was the dynamic confined compression creep test. This test was found to be useful to define the inherent time-dependent mechanical characteristics of bone grafts.6

**MATERIALS AND METHODS**

**Materials**

The human morsellized bone grafts tested in this study were made of freshly frozen human femoral heads stored at −80 °C. After thawing, all soft tissues were removed from the femoral heads. The femoral heads were milled by the Noviomagus mill (Howmedica International Ltd., Staines, UK), with the use of the finest rasping blade. This resulted in bone grafts with an average diameter of 2.1 ± 1.3 mm, consisting of cancellous and cortical bone (Figure 1). Eight specimens of 4 g each were tested.

With respect to the TCP/HA biomaterial particles (Howmedica International Ltd., Staines, UK), various compositions of particles were tested. The reference biomaterial group was the one with small (3–5 mm) biomaterial particles with a TCP:HA ratio of 80:20 and 0% porosity (Figure 2). Three other combinations were tested varying in TCP:HA ratios, particle sizes and porosities (Table I). To test the effect of the parameter TCP:HA ratio, particles with a ratio of 80:20 and particles with a ratio of 20:80 were tested (2 vs. 3 in Table I). The size effect was determined by testing small (3–5 mm) and large (6–8 mm) particles (2 vs. 5 in Table I). With the use of particles with 0% or 50% porosity, the effect of particle porosity was tested (2 vs. 4 in Table I). Biomaterial groups 3, 4, and 5 each differed from the reference group with regard to one of the three mentioned parameters. Before testing, the particles were soaked in a saline solution for half an hour. Each group consisted of eight specimens of 4 g each. In addition, two groups were made by 50:50 weight mixtures of biomaterial particles and human morsellized allografts (Table I). The human morsellized allografts were mixed with particles of the reference group, and with 50% porosity particles.

**Methods**

To define the time-dependent deformational behavior of the specimens, dynamic confined compression creep tests were applied. After preparing and weighing the specimens, they were manually impacted in the impermeable cylindrical test chamber with a diameter of 20 mm (Figure 3). A rigid, porous filter was placed on top of the impacted material, allowing free fluid exudation during loading. On top of the filter, a load spreader ensured that the applied load was equally distributed over the whole surface of the specimen. With the use of a servo-hydraulic MTS testing machine, a dynamic force, ranging from 10 N (min. force) to 840 N (2.68 MPa, max. force), was applied with a frequency of 1 Hz for a period of 900 s (loading phase). This load level was chosen as it resembles the stress level that may be expected around cemented cups7 and femoral implants.8 The minimum load was 10 N to
ensure contact with the surface of the specimen. After this loading period, the specimens remained unloaded for another 900 s, allowing the fluid exudate fluid to be sucked back into the specimen. The deformation and recovery of the impacted material was measured by an extensometer (resolution about 2 μm), connected between the loading rod and the specimen. With 11-s time intervals, the force displacement signals during a 1.2-s period were sampled and stored in a PC.

The following formula was used to calculate the strain:

\[ e(t) = \frac{h_{\text{min}}(t)}{h_0} \ln \frac{h_{\text{min}}(t)}{h_0} \]

where \( e(t) \) is the true strain, which is calculated with the instantaneous length rather than the original length, \( h_{\text{min}}(t) \) is the height of the specimen at minimum force at \( t \) seconds, and \( h_0 \) is the initial height of the specimen at \( t=0 \) seconds. The total strain (strain at the end of the loading phase) represents the deformational behavior of a material after dynamic loading. The recovery strain (strain at the end of the loading phase minus strain at the end of the unloading phase) will be presented in the results as a percentage of the total strain.

The elastic modulus of a specimen was determined by the ratio of cyclic stress and cyclic strain:

\[ E = \frac{h_{\text{max}}(t) - h_{\text{min}}(t)}{h_{\text{min}}(t)} \]

where \( h_{\text{max}}(t) \) is the height of the specimen at maximum force at \( t \) seconds. The elastic modulus represents the stiffness of a material. To investigate if the stiffness of a material changed

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**TABLE I. General Overview of All Tested Series**

<table>
<thead>
<tr>
<th>Group</th>
<th>Composition</th>
<th>Porosity</th>
<th>Size (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Human femoral bone (cortical and cancellous)</td>
<td>NA</td>
<td>2.1 ± 1.3</td>
</tr>
<tr>
<td>2</td>
<td>TCP:HA = 80:20</td>
<td>0%</td>
<td>3–5</td>
</tr>
<tr>
<td>3</td>
<td>TCP:HA = 20:80</td>
<td>0%</td>
<td>3–5</td>
</tr>
<tr>
<td>4</td>
<td>TCP:HA = 80:20</td>
<td>50%</td>
<td>3–5</td>
</tr>
<tr>
<td>5</td>
<td>TCP:HA = 80:20</td>
<td>0%</td>
<td>6–8</td>
</tr>
<tr>
<td>6</td>
<td>Mix group 1 and 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Mix group 1 and 4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Figure 2.** Biomaterial particles, TCP:HA = 80:20, 3–5 mm, 0% porosity.

**Figure 3.** Test chamber.
in time during this test, the elastic modulus was determined at the beginning and at the end of the loading phase.

The last parameter that was determined in this study is the amount of hysteresis in the cyclic stress/strain relationship, which is a typical phenomenon of a viscoelastic material. The viscous part of the mechanical behavior makes the response of a material to loading time dependent. Hysteresis surface areas were determined at the beginning, in the middle, and at the end of the loading phase. By considering these three points in time, a potential difference in the energy dissipated in time could be seen.

The effects of the material parameters on the measured quantities were statistically analyzed with the use of student’s t tests with a significance level of \( p = 0.05 \).

**RESULTS**

The human bone graft specimens (Group 1) showed the highest deformation at the end of the loading phase (Table II). The total strain of 0.46 was significantly higher than the total strain of all other groups. The recovery strain of the human grafts, about 27% relative to the total strain, was also significantly higher compared to the other groups. The biomaterial particles (Groups 2–5) produced the smallest deformations. Within the biomaterial groups, porosity and graft size significantly influenced the total strain and the recovery strain. The total strain was increased by larger particles and higher particle porosity, whereas the recovery strain decreased (Table II; Figure 4). Despite these effects the deformation pattern was still remote from that obtained with the human graft material. The TCP:HA ratio of the biomaterial particles did not significantly influence the total strain or the recovery strain. The mixtures (Groups 6 and 7) produced intermediate deformation patterns, with Group 7 showing significantly more deformation than Group 6. A 50:50 weight mixture resulted in an intermediate deformation pattern.

With respect to the stiffness of a material, the human bone grafts showed the smallest elastic modulus, about 135 N/mm\(^2\), at the end of the loading phase (Table II). All other groups showed a significantly higher elastic modulus. The highest elastic moduli were found for Groups 2–4; they are about 520 N/mm\(^2\). Larger particles (Group 5) significantly decreased the elastic modulus to 439 N/mm\(^2\). The mixtures showed again intermediate patterns with no difference between Groups 6 and 7. However, a 50:50 weight mixture did not result in a proportional change in elastic modulus. These mixtures behaved more like the human bone grafts than like the biomaterial particles. All groups showed an increasing elastic modulus toward the end of the loading phase. Hence, the materials became stiffer during the tests.

Group 1, the human bone grafts, showed the highest energy dissipation during one loading cycle (Figure 5). All other groups showed significantly less energy dissipation. The TCP:HA ratio was the only material parameter of the biomaterial particles that influenced the energy dissipation, although it is questionable whether the biomaterial particles showed any hysteresis behavior at all (Figure 5). The mixtures showed more energy dissipation than the biomaterial particles, but less than the human bone grafts. However, the energy dissipation of the mixtures was still relatively small. Mix 1 (Group 6) did not differ from Mix 2 (Group 7). The energy dissipation was determined at the beginning, in the middle, and at the end of the loading phase. When these three points in time are compared, all groups showed a decreasing energy dissipation in time, indicating the loss of viscoelastic capacity.

**TABLE II. Averaged Parameters for the Seven Testing Series. Standard Deviations Are Shown in Brackets. The Recovery Strains are Given as Percentages of Total Strain. The Values for Groups 2–7 for All Parameters Differed Statistical Significantly from Those of Group 1. Significant Differences of the Parameters of Groups 3–7 Relative to Group 2 Are Indicated with a * .**

<table>
<thead>
<tr>
<th>Group</th>
<th>Total Strain (Average, SD)</th>
<th>Recovery Strain (Average, %)</th>
<th>E-Modulus (N/mm(^2), Average, SD)</th>
<th>Energy Density (KPa, Average, SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.455 (0.0273)</td>
<td>27.0</td>
<td>84.6 (25.3)</td>
<td>134.7 (28.1)</td>
</tr>
<tr>
<td>2</td>
<td>0.0859 (0.0166)</td>
<td>4.6</td>
<td>442.4 (49.2)</td>
<td>524.7 (56.2)</td>
</tr>
<tr>
<td>3</td>
<td>0.101 (0.0166)</td>
<td>2.4</td>
<td>514.3 (53.1)</td>
<td>0.760 (0.250)</td>
</tr>
<tr>
<td>4</td>
<td>0.196* (0.0117)</td>
<td>1.0*</td>
<td>479.0 (74.7)</td>
<td>0.773 (0.313)</td>
</tr>
<tr>
<td>5</td>
<td>0.126* (0.0381)</td>
<td>2.0*</td>
<td>386.6* (21.5)</td>
<td>1.03 (0.356)</td>
</tr>
<tr>
<td>6</td>
<td>0.288* (0.0271)</td>
<td>20.6*</td>
<td>198.3* (27.0)</td>
<td>5.97* (1.11)</td>
</tr>
<tr>
<td>7</td>
<td>0.336* (0.0200)</td>
<td>23.4*</td>
<td>188.9* (16.1)</td>
<td>6.03* (0.746)</td>
</tr>
</tbody>
</table>

Figure 4. Strain curves of all tested series.
MECHANICAL PROPERTIES OF HA/TCP PARTICLES

DISCUSSION

Biomaterials are attractive as substitutes for bone allografts to be used with the impaction grafting technique, particularly in geographical areas where these allografts are scarce. However, before they can be applied, the materials have to be tested with respect to their mechanical and biological behavior. In this study the initial mechanical behavior of biomaterial particles was tested in comparison with the behavior of morsellized allografts.

Although the confined compression creep test was considered adequate to determine the material parameter strain, stiffness, and viscoelasticity, the test has several limitations that should be taken into account before the results can be interpreted adequately. The graft materials were manually impacted. The total strain of a material will depend on the grade of impaction. When the material is impacted firmly before testing, the total strain will be less than generated with only mild impaction. In this study all specimens were prepared and impacted by the same person to minimize the variation in impaction grade. Judging from the standard deviations within the groups, variations due to variable impaction were relatively small. Another limitation was the size of the testing chamber relative to the size of the graft materials. Smaller grafts may have had a more efficient positioning in the chamber at the beginning of the test in comparison with the larger grafts. The positioning of the grafts might influence the deformation pattern during the test. However, one should realize that in real revision cases defects of the size of the testing chamber are not uncommon, indicating that inadequate positioning of relatively big particles may also happen clinically. In this study no cement was added to the grafts, although the clinical experience is based on cemented cup and femoral components with impacted grafts in reconstructive surgery. Hence, cement–bone graft interaction was not included in this study. In this experiment saline was added to the biomaterial particles according to the instruction of the manufacturer, whereas the human bone graft particles contain marrow and blood. The difference in the fluid part of the materials will affect the viscoelastic response.

With respect to the total deformation at the end of the loading phase, the biomaterial particles showed less deformation than human bone grafts. However, the material parameters of particle size and particle porosity seemed important factors for the total deformation. Larger particles and, more significantly, porosity increased the total deformation. Apparently the porous particles must have undergone some microdamage at locations where the particles supported each other, although damage at a macroscopic level was not noted.

Although the human bone graft group was considered as the reference group in this study, it should be mentioned that the mechanical behavior of morsellized human bone chips is certainly not standardized yet. A large number of studies are in progress and have recently been published to investigate the effects of all kinds of parameters (such as graft size, water/fat contents of the grafts, bone mill type, implantation grade, and graft preparation) on the mechanical response of the bone graft layer. All these parameters show some effect on the mechanical behavior of the graft layer.

The mixtures of human grafts and biomaterial particles are the groups that were closest to the mechanical behavior of the human bone grafts. Within these mixtures, the particle porosity influenced the total deformation. In the literature, mixtures of human bone grafts and biomaterials showed better results than biomaterial particles alone. The bone ingrowth of biomaterial particles in vivo will be better when the particles are mixed with human bone grafts. Moore, Chapman, and Manske showed that the ingrowth of 100% TCP and HA in the host bone is not very satisfying, but mixing with human bone grafts gave excellent results.

One could argue that because of the good results obtained with human allografts used as graft material in revision surgery, the hypothesis can be adopted that the biomaterial that approaches the mechanical behavior of the human bone grafts most closely is the most optimal one. There is then the question of what the parameters (TCP:HA ratio, particle size and particle porosity) of biomaterial particles should be to mimic the mechanical properties of human bone grafts as realistically as possible. This study indicates that the particles should be relatively large and porous. However, the mech-
ical behavior of these particles is so remote from that of the human bone grafts that a similar mechanical behavior of the current tested HA/TCP particles cannot be obtained. Hence, from that perspective no preferred combination of particle characteristics can be recommended.

Nevertheless, based on this study the response of these particles to a dynamic mechanical load is characterized and offers the possibility of answering the questions posed in the Introduction. The particles did not crunch under impaction, nor were they damaged to any significant level, nor did they show relative sliding under the cyclic stress of 2.68 MPa. Hence, it can be expected that the defect can be filled and impacted with the particles without significant damage of the particles. Cement penetration through the inter-particle space is not hampered by (partly) damaged particles allowing for a stable cemented reconstruction. The elastic and viscoelastic deformation of the biomaterial particles was very small. This indicates that particles used to fill a defect act rather rigidly. This may lead to rather high local stresses between the particles and the surrounding tissue. In addition, the biphasic behavior is virtually absent, indicating that fluid flow around the particles may be low, resulting in a delay of incorporation of the biomaterial particles. Mixing the particles with human bone graft gave the graft some more flexible and viscoelastic behavior.

In conclusion, this study showed that the mechanical behavior of HA/TCP biomaterial particles was remote from that of human bone grafts. The most important difference may be viscoelastic behavior, which is virtually absent with the biomaterial particles. Therefore, this study suggests that the application of these HA/TCP biomaterial particles should be done with great care. It may be worthwhile to consider mixtures of biomaterial particles and morsellized allografts as a compromise to optimize the mechanical properties and to minimize the amount of human material required. Animal models should prove that the biological response to these particles or particles/bone graft mixtures is adequate before they are clinically used in revision surgery.

The biomaterial particles were donated by Stryker Howmedica Osteonics, Newbury, UK.

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