Tuning the Degradation Rate of Calcium Phosphate Cement via Addition of PLGA Porogen Content to Accelerate Bone Regeneration

CIA van Houdt[1], RS Preethanath[2], BAJA van Oirshot[1], JA Jansen[1], JJJP van den Beucken[1]
[1.] Department of Biomaterials, Radboud University Medical Centre, Nijmegen, The Netherlands.
[2.] College of Dentistry, King Saud University, Riyadh. Kingdom of Saudi Arabia.

Statement of Purpose:

Calcium phosphate cement (CPC) is a widely used bone substitute material to fill bone defects in several fields of reconstructive surgery, due to the biocompatibility and osteoconductive properties. Bone substitution can also be applied to increase the amount of bone around metallic implants, to stimulate bone growth, and to improve implant survival[1]. To overcome the disadvantage of the slow degradation rate of CPC, substantial efforts have focused on combining CPC with a rapidly degrading component, such as polylactic-co-glycolic acid (PLGA)[2]. Incorporation of PLGA into the cement allows for rapid pore formation, which increases surface area and allows for bone ingrowth. The characteristics of the PLGA porogens have been proven critical for the CPC/PLGA degradation rate as well as the bone forming capacity[2,3]. Specifically, hollow and dense microspheres with variations in molecular weight, chemical modifications of PLGA end-groups, and dimensions have been evaluated for their effects on degradation and bone formation[2]. For clinical applications, however, a more cost-effective PLGA porogen fabrication method is mandatory. Consequently, the aim of this study was to evaluate the degradation and bone forming capacity of CPC/PLGA composites with cryo-milled PLGA particles at two different amounts in a rat femoral condyle defect.

Methods:

Twenty-one male Wistar rats received titanium implants surrounded by pre-set CPC/PLGA. Two ratios of CPC/PLGA were used (50/50 and 70/30 wt.%) and implanted alternating left and right in the femoral condyle. The cryo-milled PLGA particles size ranged from 0-150 µm. Histomorphometrically, we analyzed material degradation, new bone formation and bone-to-implant contact (BIC%) after 4 and 8 weeks. Statistical analysis was performed using GraphPad Prism 5 using a Student's t-test at a level of significance of $p<0.05$.

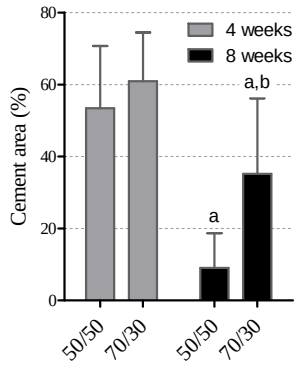

Figure 1. Cement area in the region of interest (mean +SD). [a] p<0.001 compared to 4-week equivalent; [b] p<0.001 compared to 8-week 50/50.

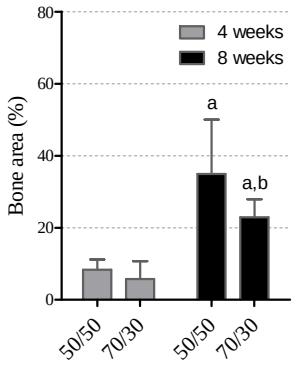

Figure 2. Bone area in the region of interest (mean +SD). [a] p<0.001 compared to 4-week equivalent; [b] p<0.05 compared to 8-week 50/50.

Results:

The results showed a significant decrease in cement of both materials, comparing the two time points 4 to 8 weeks ($p<0.001$). The 50/50% CPC/PLGA degrades faster compared to 70/30% CPC/PLGA. The difference in degradation is significant after 8 weeks ($p<0.001$), but not after 4 weeks.

There was a significant increase of bone after degradation of both materials within the region of interest comparing the results after 4 and 8 weeks ($p<0.001$). The area of newly formed bone was higher for 50/50% CPC/PLGA compared to 70/30% CPC/PLGA. The difference was significant after 8 weeks ($p<0.05$), but not at 4 weeks.

Increasing the degradation rate by increasing PLGA content from 30 to 50% resulted in 1,5 fold more bone formation after 8 weeks. Bone forming capacity calculations showed that for 1% degraded material of 50/50% CPC/PLGA results in 0,67% new bone replacement, compared to 0,60% for 70/30% CPC/PLGA.

Degradation of both materials led to similar marginal bone-to-implant contact values after 8 weeks of implantation (range: 11.69-11.89%). The increase of BIC% between 4 and 8 weeks was significant for 70/30% CPC/PLGA ($p<0.05$), but not for 50/50% CPC/PLGA.

Conclusions:

These data demonstrate a correlation between the degradation rate of CPC/PLGA and new bone formation. Tuning the degradation rate of CPC/PLGA by increasing PLGA porogen content in resulted in enhanced bone formation.

References:

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