Enhanced Bioactivity of PEEK by Accelerated Neutral Atom Beam Technique

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Statement of Purpose: Polyetheretherketone (PEEK) has become a popular material for use in orthopedic applications but has several drawbacks that limit its effectiveness *in vivo*. While PEEK is biocompatible, radiolucent, and similar in elasticity to bone, it has been shown to be inert and does not integrate well with bone. Current efforts are focused on increasing the bioactivity of PEEK using surface modifications to improve the bone-implant interface. We have employed a novel Accelerated Neutral Atom Beam technique (ANAB) which enhances the bioactivity of PEEK by generating a shallow surface modification without adding a coating to the surface. ANAB employs an intense beam of cluster-like packets of accelerated unbonded neutral argon (Ar) gas atoms. These beams are created by first producing highly energetic gas clusters comprised of van der Waals bonded Ar atoms, transferring energy to the clusters to cause release of most of the interatomic bonds, then deflecting away any remaining electrically charged clusters of bonded atoms. ANAB treatment of PEEK results in nanometer scale surface modification of PEEK and an increase in surface hydrophilicity. Human osteoblasts seeded onto ANAB-treated PEEK exhibit enhanced growth as compared to control PEEK as shown by cell proliferation assays and microscopy. Gene expression studies have shown that osteoblasts seeded on ANAB-treated PEEK exhibit the same levels of osteoblastic differentiation seen on tissue-culture plastic. An in vivo study using a rat calvarial critical size defect model revealed enhanced osseointegration with bone growth only on ANAB-treated PEEK and not on the untreated control. These data strongly suggest that ANAB treatment of PEEK has the potential to enhance its bioactivity to result in enhanced bone formation and decrease osseointegration time of orthopedic and spinal implants.

Methods: PEEK film disks of 1cm Ø were treated with ANAB at 5e16 Ar atoms/cm2 or left as controls. Atomic force microscope (AFM) measurements were performed in non-contact mode for 1µm regions (Park Systems XE-70) and R_a and R_z measurements were calculated. Contact angle was measured using the sessile drop method on a manual simplified device as described by Lamour et.al. (2010) and droplet angles were measured by ImageJ software (NIH) with the contact angle plugin. For proliferation studies, human osteoblasts (2000/cm^2) were seeded onto the surface and allowed to proliferate for 14 days. Disks were then stained with crystal violet, visualized by light microscopy, and eluted to measure absorbance, inferring cell number. Gene expression studies were performed by real time PCR for alkaline phosphatase (ALPL) and osteocalcin (BGLAP) and corrected with GAPDH. An in vivo study using a rat calvarial critical size defect model was done to show bone growth on the surface of ANAB-treated and –untreated PEEK disks 3mm Ø, 1 mm thick. 4 weeks after implantation, histology was performed to determine the amount of bone re-growth on the surface.

Results: AFM measurements on ANAB-treated PEEK revealed nano-scale surface texturing which was not seen on the controls. The texturing is in the range of 20-50nm with a depth of only 5nm, leaving the R_a and R_z unchanged. By contact angle measurements, we found that ANAB greatly increases the surface hydrophilicity of PEEK (θ=36.1°) as compared to controls (θ=76.4°). PEEK processed by ANAB exhibits a significant increase in osteoblast proliferation by day 14 (absorbance = 1.07±0.19) as compared to control samples (0.13±0.03, $p<0.001$).

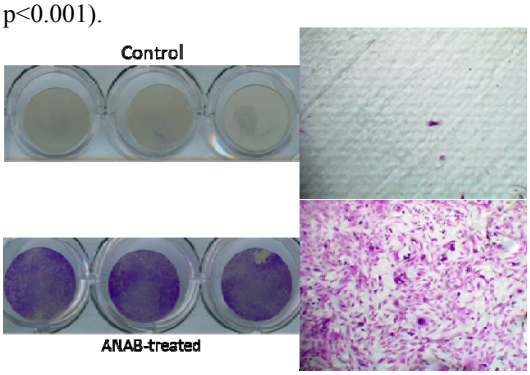

Figure 1. Cell proliferation on PEEK film.

As cells do not attach and grow well on native PEEK, gene expression analysis from RNA isolated on day 14 from ANAB-treated PEEK was compared to Tissue Culture Polystyrene (TCPS). Gene expression analysis revealed up-regulation of ALPL on both surface by about 16-fold, there was no significant difference between the materials (p=0.234). BGLAP gene expression was also up-regulated on both materials by approximately 7 fold with no difference between ANAB-treated PEEK and TCPS (p=0.114). The rat calvarial defect model showed that ANAB-treated PEEK resulted in a bone ledge growing over the top of the disk and covering approximately 50% of the surface. The control PEEK disk had no bone coverage and resulted in formation of fibrous tissue. Control PEEK displayed the beginning of bone resorption on the sides of the disks whereas good bone purchase is seen on ANAB-treated disks.

Conclusions: ANAB results in a nano-scale texturing and improved hydrophilicity on otherwise chemically resistant PEEK. The resulting processing of PEEK by ANAB significantly enhances osteoblast cell attachment and proliferation. ANAB treatment of PEEK increases the cytoactivity of PEEK to match that of TCPS. Enhanced osseointegration was demonstrated in the in vivo study where bone formation was evident only on the ANAB treated PEEK. Taken together, these data strongly suggest that ANAB treatment of PEEK enhances bone formation and may significantly decrease osseointegration time for orthopedic implants.