Accelerated Neutral Atom Beam Processing Improves PEEK In Vivo Osseointegration

Joseph Khoury, PhD[1], Cathy Tkaczyk, PhD[2], Art Kurz[1], James Bachand[1], Richard Svrluga[1], Michel Assad, PhD[2].
[1]Exogenesis Corp, Billerica, MA, USA, [2]AccelLAB Inc, Boisbriand, QC, Canada.

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Introduction: Polyetheretherketone (PEEK) has gained popularity for many orthopedic applications but has significant limitations. PEEK is biocompatible, similar in elasticity to bone, and radiolucent; however, PEEK is inert and does not integrate well with bone [1]. Current efforts focus on increasing the bioactivity of PEEK with surface modifications, including coatings, to improve the bone-implant interface. We have developed a novel accelerated neutral atom beam technology (ANAB) that can modify the surface of an implantable medical device to a depth of no more than 2-3nm [2]. ANAB employs a directed beam of neutral gas atoms, which have average energies controlled over a range from a few electron volts (eV) to over 100eV per atom. ANAB leaves no residues in or on the material surface, therefore no coatings to delaminate. Initial in vitro studies showed significant increases in cell proliferation and osteogenic differentiation of mesenchymal stem cells into osteoblasts growing on ANAB-treated PEEK as compared to controls [3]. In this study, we evaluated the in vivo osseointegration and bioactivity of ANAB-treated PEEK using an ovine femoral and tibial insertion model.
Methods: Medical grade PEEK rods (Solvay Plastics) were machined into 4 mm diameter cylindrical implantable rods measuring either 15 or 24mm in length (cancellous and cortical bone implantations, respectively). The PEEK implants were further modified with a series of macroscopic pores (1 mm3 gaps or pits) as available void spaces created in order to fully demonstrate the extent of osteoid progression; implants used for biomechanics were not modified. Half of the devices were then treated by ANAB (1x10e17 argon atoms per cm2), the remaining implants were kept as untreated controls. All surgical procedures and animal husbandry adhered to protocols approved by AccelLAB's IACUC, an AAALAC fully accredited institution. In order to evaluate new bone formation and implant-to-bone apposition, six adult female dorset sheep (≥ 12 months) underwent bilateral surgery on femurs and tibiae. Implants were placed in the cortical region of the mid-femur (n=2 per group/implantation time), the cancellous region of the distal femur (n=2), and the cancellous region of the proximal tibia (n=2). All implants were press-fitted with a 2 mm protrusion for alignment. Following surgical procedures, the animals were allowed to recover with full weight bearing and were then assigned to either a four-week or twelve-week implantation period with daily health checks. Following necropsy, PEEK explants and surrounding bone from the left hindlimbs were imaged by µCT (Skyscan 1172) and reconstructed into 3D images. The samples were then processed for non-decalcified bone histology using Exakt microgrinding and Goldner's Trichrome stain. The contralateral PEEK explants and surrounding bone from the right hindlimbs were assayed by a static push-out test using an Instron ElectroPuls E3000 in order to establish the stiffness (N/mm2), peak load (N), and interface strength (kPa).
Results: Following a 4-week implantation period, µCT reconstruction of the ANAB-treated implants showed excellent bone remodelling in absence of adjacent bone density differences. Following

histology, the ANAB-treated implants (Figures 1B and F) also demonstrated a direct bone apposition and initiation of bone growth into the PEEK gaps/pits. In contrast, under μCT, the untreated PEEK controls revealed a thickened appearance of bone callous surrounding the implant that may be indicative of soft tissue and fibrosis; histological analysis later confirmed bone resorption and fibrous tissue presence around the control implants (Figure 1A and E). At the 12 week time-point, both histology and μCT imaging showed a clear osseointegration on ANAB-treated PEEK implants with an osteoid front colonizing the created voids, as opposed to the untreated-implants, which lacked any bony ingrowth (Figures 1 and 2). Moreover, histomorphometry results of ANAB-treated devices in cancellous bone at 12 weeks revealed a 3.09-fold increase of the percentage of bone apposition as compared with controls ($p<0.014$). For implants inserted in cancellous bone, biomechanic push-out testing carried out at 4 weeks revealed an enhanced bonding between ANAB-treated implants and adjacent bone resulting in a 2.14-fold stiffness versus untreated PEEK ($p<0.003$, Figure 3A). In addition, an increased implant-to-bone interface strength by 94.9% was observed ($p<0.04$, Figure 3B) when compared to controls. Similarly, following 12 weeks of implantation, ANAB-treated implants in cancellous bone demonstrated an increased bonding stiffness to 2.17 fold ($p<0.04$, Figure 3C) and improved implant-to-bone interface strength by 107.6% compared with controls (Figure 3D). In cortical implants, while no discernible differences were noted at 4 weeks post-implantation, the 12 week time-point revealed an increased stiffness of treated implants by 2.32 fold as compared to controls and improved implant-to-bone interface strength by 69.6% versus untreated PEEK.

Discussion: PEEK has become a material of choice for many orthopedic applications, however the strategies to promote osseointegration remains a challenge. Numerous research teams have attempted to modify PEEK surface properties using a variety of means including surface modifications such as plasmas, chemical modifications, surface coatings, including the addition of hydroxyapatite, as well as physical modifications such as porous PEEK. Most of these modifications have shown limited in vitro success [4]. In order to overcome the inert characteristics and to significantly improve the osseointegration of PEEK, this ovine model has shown an enhanced bone apposition and bone void ingrowth on ANAB-treated PEEK implants as compared with untreated PEEK devices. Both μCT and histology illustrated the limitations of untreated PEEK as an implant material with the presence of fibrous tissue with an impact on bone-to-implant strength, which may lead to potential implant failure. On the contrary, the ANAB-treated PEEK resulted in enhanced bone apposition from an early time point and lead to bone void ingrowth (Figure 1D, 2B). This bone apposition and integration were also reflected in significantly enhanced mechanical strength between the treated implant and the surrounding bone. Therefore, ANAB treatment of surfaces results in surface modifications which encourage osteoblast cell attachment, proliferation, and differentiation observed during the osseointegration process [3]. ANAB is not a coating and has nothing to delaminate from the surface. Because ANAB is less than 3-nm deep, the bulk properties of PEEK are not affected, leaving the overall strength, elasticity, and radiolucency unchanged. ANAB surface modification results in bioactive PEEK, which promotes osseointegration.

Significance: PEEK is a material of choice in orthopedics, it is however inert and does not integrate well with bone. Attempts at improving the bioactivity of PEEK using plasma treatments, chemical etching, hydroxyapatite coatings, and porosity creation have inherent limitations and absence of osseointegration. In this study, we have demonstrated that surface modification of PEEK by ANAB

results in a surface which encourages bone in vivo ongrowth and ingrowth without changing PEEK's desirable aspects.

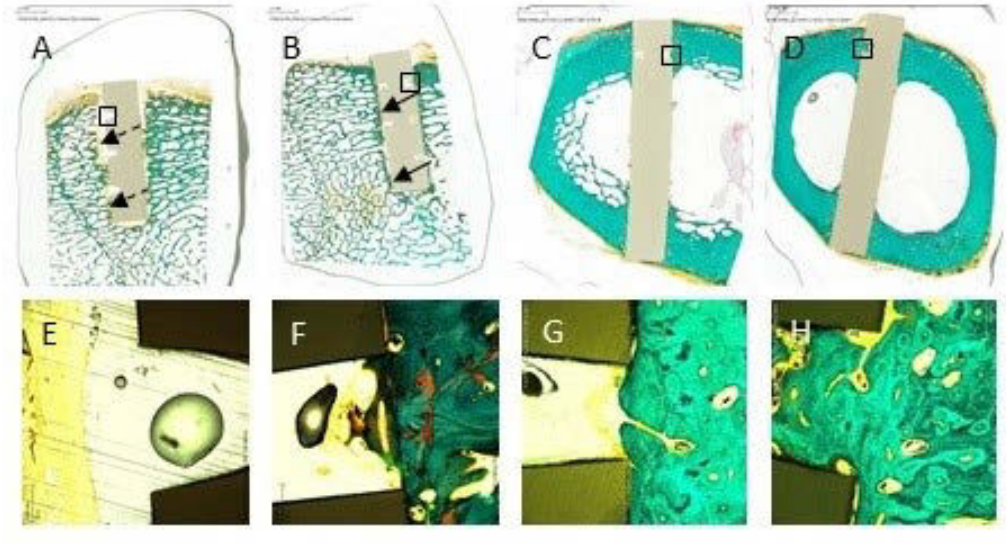

Figure 1. Goldner's Trichrome stain on distal femur cancellous and mid-shaft femoral cortical bone with PEEK implants. Four-week whole mount images show bone (green) resorption and fibrous tissue (yellow) invasion (dashed arrows) of cancellous control implants (A) and direct bone apposition (solid arrows) on ANAB-treated implants (B). Higher magnification images (boxed area in A and B) at the pits reveals fibrous tissue adjacent to the control implant (E) and bone ingrowth into pores of treated implants (F) also revealing new bone formation stained in orange. At 12 weeks, cortical bone shows little void fill on controls (C and G) while nearly complete void fill is seen on ANAB-treated implants (D and H).

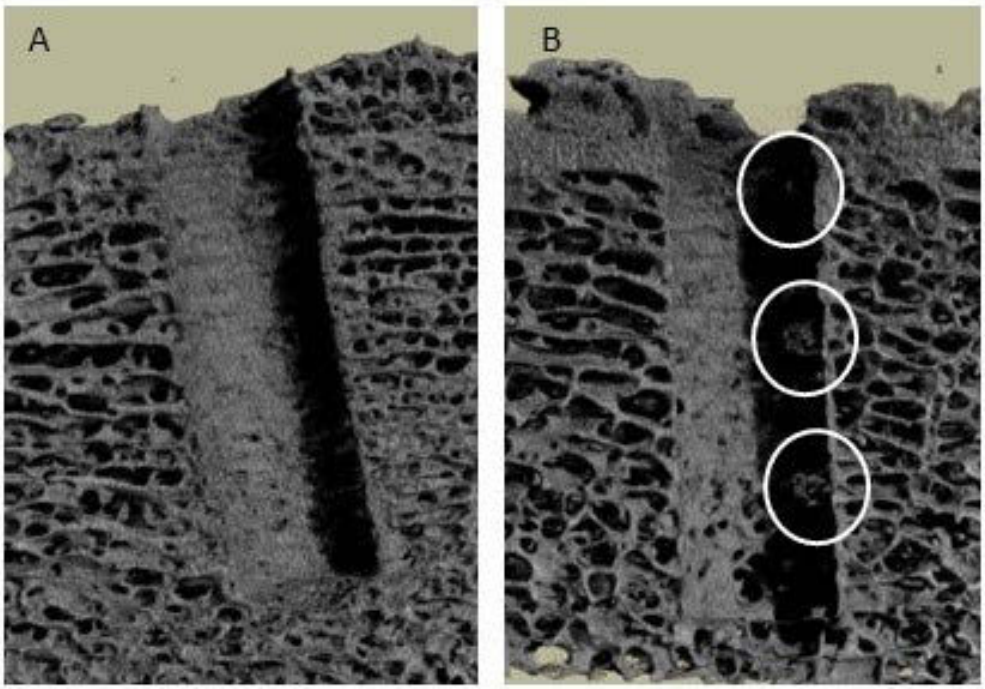

Figure 2. µCT reconstruction of radiolucent PEEK and surrounding bone, control (A) and ANAB-treated PEEK (B). Bone growing into the gaps are seen on the ANAB-treated implants indicated by the white circles (B), which is absent with controls (A).

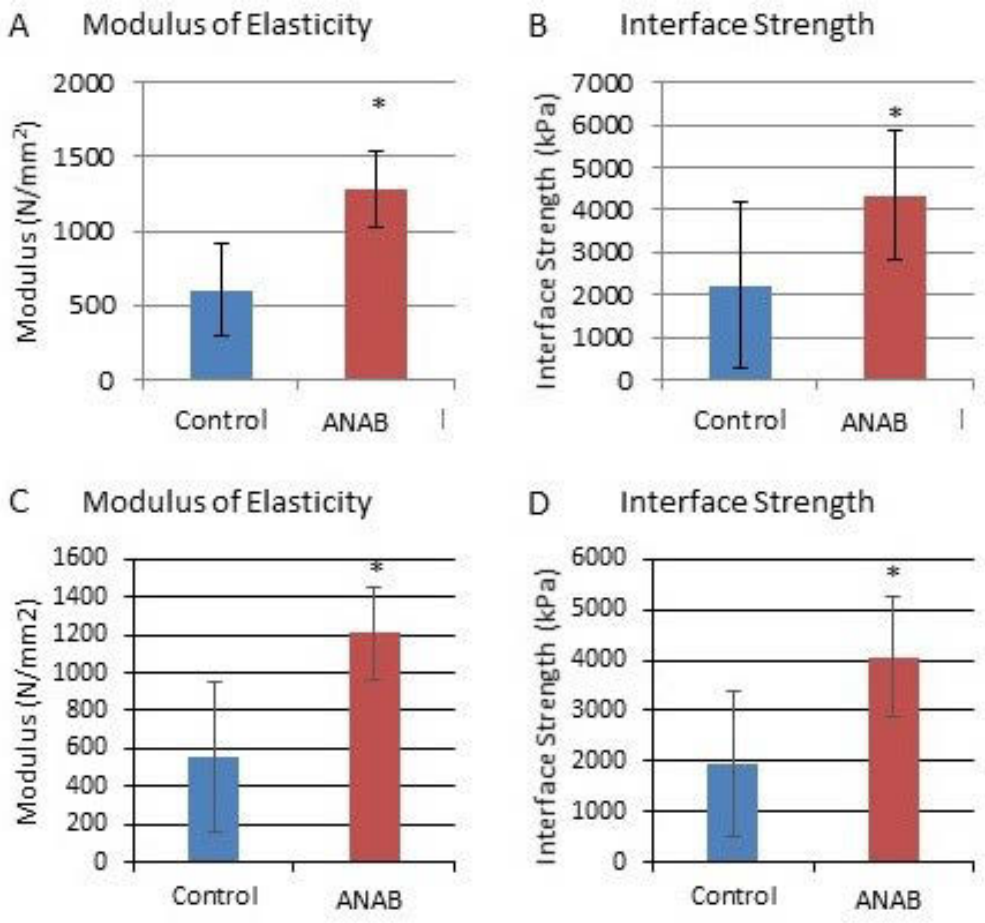

Figure 3. Biomechanical strength between implants and cancellous bone increases significantly on ANAB-treated implants as compared to controls. Significant changes (* $p<0.05$) were observed at both 4 week (A, B) and 12 week time-points (C, D): this is reflected by implant-to-bone stiffness (A, C) and bone-to-implant interface strength (B, D) on ANAB-treated implants as compared with controls.