Crucial Role of Periosteum in Peri-implant Bone Formation around Diaphyseal Engaging Implant

Vincentius J Suhardi, Anastasia Oktarina[1], Andrew Thomson, Juergen Alphonsus[2], Matthew B Greenblatt[3], Lionel B Ivashkiv[1], Mathias P G Bostrom[1], Xu Yang
[1]Hospital For Special Surgery, [2]Orthopedic Surgery, [3]Weill Cornell Medical College

INTRODUCTION:

Diaphyseal-engaging implants after osseous resection at diaphyseal level are commonly used in revision arthroplasty (e.g., proximal femur replacement, distal femur replacement)[1], oncology reconstruction[2], and percutaneous osseointegrated prostheses (POP) after amputation[3]. Peri-implant bone formation (osseointegration) is crucial for securing these implants, which is a critical factor for the success of the surgical procedure. When bone fails to properly form around these implants, peri-implant fibrous tissue formation can result in instability, frequently requiring revision surgery. While the role of the periosteum in fracture healing is well established, there is currently a knowledge gap regarding the role of the periosteum in peri-implant bone formation. In this study, we highlight the crucial role of the periosteum around the diaphyseal resection site for peri-implant bone formation. Eradication of the periosteum around the resection site resulted in the inhibition of peri-implant bone formation and the induction of peri-implant fibrosis.

METHODS:

LepR-creERT mice was a kind gift from Dr Bo Zhou from Shanghai Institute for Biological Sciences. Rosa26-CAG-loxp-stop-loxp-tdTomato (Stock 007909) was purchased from Jackson Laboratories.

Model of transfemoral amputation: A circumferential incision with posterior skin flap was made around distal 1/3 of femur. Major vessels were cauterized. Femoral and sciatic nerves were resected. The femoral shaft was resected transversely just distal to the mouse third trochanter. The intramedullary canal was retrogradely reamed to 50% larger than the diameter of the stem of a PMMA (Simplex HV) implant, resulting in a loose implant with potential micromotion and thus restricting osseointegration **(Figure 1.a)**. Special attention was placed to maintain all the power tools at ice-cold temperature with copious irrigation during osseous resection and reaming to minimize thermal damage. For the mice in periosteum removed group, electrocautery was used to remove the periosteum from the resection level to 2 mm proximal to the resection level. The implant was loosely inserted into the over-drilled canal, the quadriceps femoris muscle was sutured to the hamstring muscles, and the wound was closed.

Micro-CT: Scans (μCT 45, Scanco Medical, Switzerland) were performed at 6 μm voxel size, 90 kVp, 145 mA, and 0.36 rotation step (180 angular range) per view. Regions of interest were defined as peri-implant (cancellous bone 100 μm around the entirety of the stem). Radiological bone morphological parameters, particularly bone volume fraction (bone volume/total volume; BV/TV), trabecular number (Tb.N.), trabecular thickness (Tb.Th), and trabecular separation (Tb.S) were assessed.

Statistical Analysis: Statistical analysis was performed using Student's t-test. $p<0.05$ was considered as significant.

RESULTS:

MicroCT analysis showed statistically significant less peri-implant bone in mice with periosteum removed as compared to mice with preserved periosteum (Figure 1). In concordance with the microCT analysis, histological analysis of the peri-implant tissue demonstrated decreased peri-implant bone formation and increased peri-implant fibrous tissue formation in mice with periosteum removed as compared to mice with preserved periosteum (Figure 2a-c). Abundant pro-fibrotic, spindle-shaped LEPR+ cells were present in the peri-implant fibrous tissue in mice with periosteum removed (Figure 2d). In mice with intact periosteum, there is notable absence of peri-implant LEPR+ cells. In this group LEPR+ cells are present in the peri-sinusoidal and peri-arteriolar area as previously reported[4] (Figure 2e).

DISCUSSION AND CONCLUSION:

While the role of periosteum in fracture healing and callus formation has been well established[5], the role of periosteum for peri-implant bone formation was unclear. In this study, we showed that the periosteum plays a crucial role for bone formation around the diaphyseal resection site. Eradication of the periosteum around the resection site resulted in the inhibition of peri-implant bone formation and the induction of peri-implant fibrosis.

SIGNIFICANCE/CLINICAL RELEVANCE: Preservation of periosteum is crucial for peri-implant bone formation in diaphyseal engaging implant such as proximal femur replacement, distal femur replacement, proximal tibia replacement, POP prosthesis, and any other prosthesis that requires peri-implant bone formation with prior resection at diaphyseal level.

REFERENCES: 1, DiMartino A et al., *J Orthop Traumatol,* 2022, 23(1):18. 2, Calderon L et al., *JAAOS*, 2018, 26:e249-e257. 3, Overmann AL et al., *Biomed Eng Lett*, 2020, 10(1):5-16. 4, Zhou B et al., *Cell Stem Cell,* 2014, 15:154-168. 5, Liu Yl et al., *Developmental Cell*, 2024, 9:1192-1209.

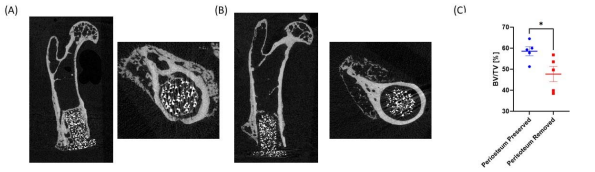

Figure 1. (A) Representative coronal (left) and axial (right) microCT of mice that underwent transfemoral amputation model with periosteum around the resection site preserved. (B) Representative coronal (left) and axial (right) microCT of mice that underwent transfemoral amputation model with periosteum around the resection site was removed. (C) BV/TV of the peri-implant bone area of mice that underwent transfemoral amputation with periosteum preserved vs removed. Data is represented as mean +/- s.d. *p<0.05.

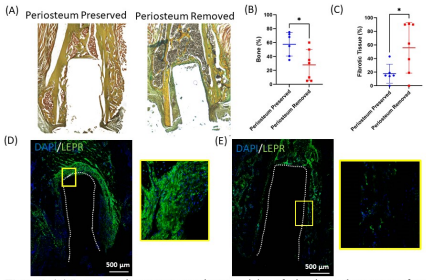

Figure 2. (A) Representative movat pentachrome staining of mice that underwent transfemoral amputation model with periosteum preserved vs removed (B-C) Histological quantification of peri-implant bone (B) and peri-implant fibrous tissue (C) in mice that underwent transfemoral amputation with periosteum intact vs eradicated. Data is represented as mean +/- s.d. *p<0.05. (D-E) Immunofluorescent imaging of mice that underwent transfemoral amputation with periosteum preserved (D) vs removed (E).