A model of open reduction fracture fixation for testing new implant surface approaches in diabetic rats

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Introduction

- Open reduction fracture fixation (ORIF) is frequently used in the treatment of ankle fractures in diabetic patients.
- However, diabetics often encounter bone resorption and adverse biological responses at the implant-tissue interface that can lead to higher implant failures[1].
- Thus, innovative and translatable approaches to improve healing post-biomaterial implantation are of the highest priority to minimize early implant loss[2].
- Previous studies have shown dicationic imidazolium-based ionic liquids (IonL) to be multifunctional coatings in Ti applications were shown to be antimicrobial[3], corrosion resistant[4] and biocompatible when tested in normoglycemic conditions[5].
- Among these criteria, it is also important to evaluate the IonL surface stability and biological interactions when inserted in bone tissue to serve as a vehicle for molecular functionalization in future orthopedic applications.
- **The goal of this project is to characterize a novel ORIF model and to explore the insertion and biocompatibility of IonL coating on Ti in diabetic conditions.**

Methods

Coating:

- Ti screws (0.76 mm x 3mm) had two different treatments: non-coated (NC-Ti) and dicationic imidazolium based ionic liquid (IonL-Ti) coated.

Animals:

- A total of 40 Lewis rats, 12-15 weeks old, were used to assess coating performance on Ti osseointegration in an ORIF model (IACUC #19-03).
- Rats were distributed into two groups of non-diabetic (ND) and diabetic (D) rats.
- For diabetes induction, 6-week-old rats were fed a high fat diet (Purina 5008) for a minimum of 6 weeks and then received an intraperitoneal injection of 55 mg/kg of streptozotocin.

Surgery:

- All rats were subjected to ORIF surgery, where a longitudinal osteotomy was made in the left tibia, followed by the placement of two Ti screws for fracture fixation.
- Healing was analyzed through microscopic (MicroCT) approaches at 2 and 21 days at 5 animals per group/time point.

Methods cont.

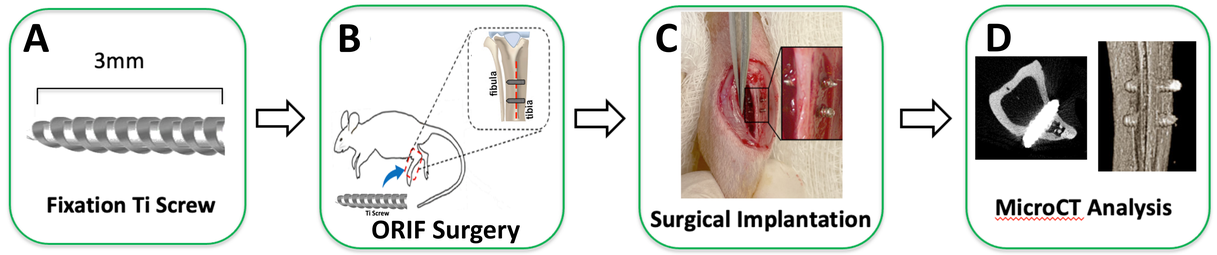

Fig 1. Representation of surgical protocol showing Ti screws (A) with open reduction fracture fixation (ORIF) surgery (B) immediately post-implantation (C) and after microCT analysis (D).

Results and Discussion

Open Reduction Fracture Fixation (ORIF) Model:

- MicroCT analysis of animals treated with NC-Ti and IonL-Ti implants revealed that the fracture defect was still present for diabetic animals at 21 days but seemed less prevalent in ND animals (Fig. 2).
- Osteotomy healing was not significantly different in animals treated with IonL-Ti implants compared to NC-Ti treatment groups based on percent of bone volume to tissue volume (BV/TV) data (Fig. 3).
- SEM images showed that IonL coating remained intact with Ti surfaces after tibial implantation (Fig. 4).

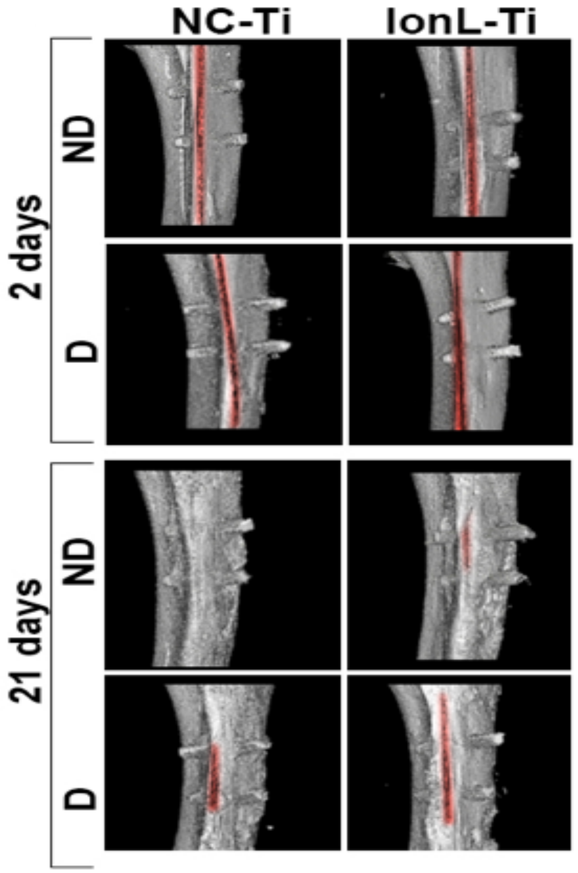

Fig 2. (MicroCT of ORIF surgery shows bone formation over time within diabetic (D) and non-diabetic (ND) groups treated with Ti screws that were uncoated (NC), and ionic-liquid coated (IonL). Red areas indicate osteotomy. All samples were analyzed at n=6 with (*) representing significant differences at p> 0.05.

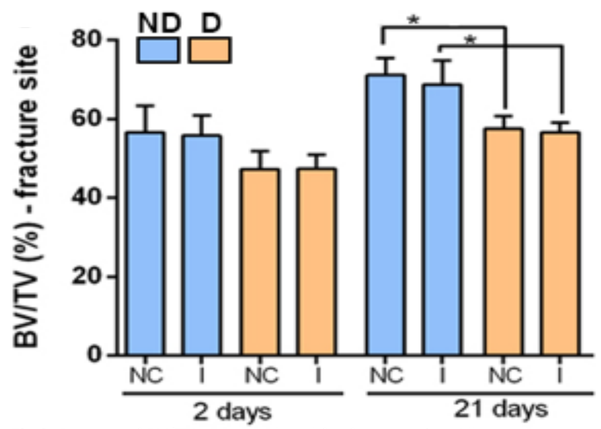

Fig 3. Percent of BV/TV were analyzed for fracture site. All samples were analyzed at n=6 with (*) representing significant differences at p> 0.05.

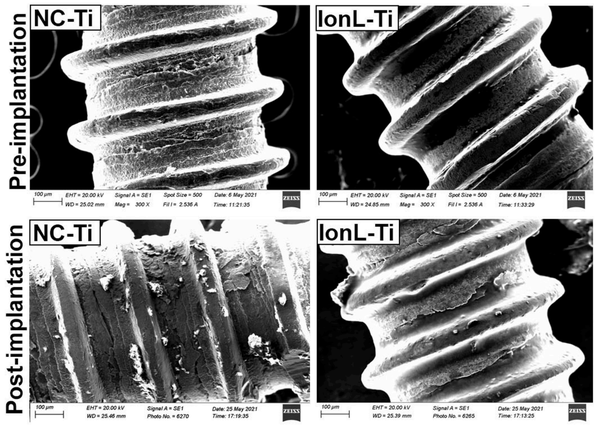

Fig 4. (A) SEM images non-coated (NC) and IonL coated screws taken pre- and post-implantation at 300x.

Conclusion

- The present study revealed that the proposed ORIF model is relevant for clinical applications seen in fracture treatments.

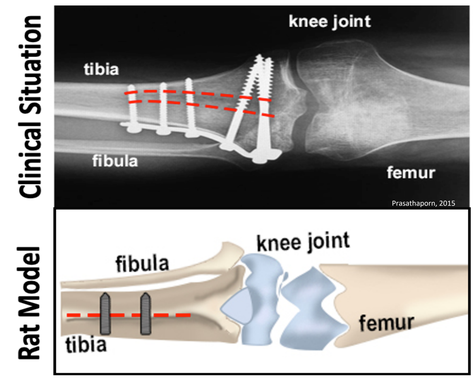

Fig 5. Comparison of clinical situation (top) and the open reduction fracture fixation (ORIF) surgery in the rat model (bottom).

- Furthermore, IonL is a promising surface coating that is biocompatible in both diabetic and non-diabetic conditions and remains stable after tibial insertion.
- This coating can be a beneficial vehicle for attachment of relevant biological molecules and functionalization of surfaces.

Future Works

- Histological analysis of decalcified bone tissues through H & E staining and immunohistochemsitry.
- Explore bone markers through ELISA and PCR.
- Immunomodulation of implant surfaces using other multifunctional coatings to promote early healing and enhance clinical performance.

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Acknowledgements

- This project is supported by the University of Texas at Dallas (UTD) Office of Research through a seed grant, Collaborative Biomedical Research Award (CoBRA).
- Ryan Margolis and Dr. Kenneth Hoyt for use of Small Animal Imaging Facility.
- This research was also supported by the NIH Ruth L. Kirschstein National Research Service Award (NRSA) Individual Predoctoral Fellowship to Promote Diversity in Health-Related Research (F31DK121483-01) Award and the Eugene McDermott Fellowship.