Optimization of a Novel Organic-Mineral Bone Adhesive

CLINICAL NEED

Although over 50% of adults over the age of 45 in the US have one or more missing teeth, only 2% of the eligible population receives a prosthetic tooth due to factors including time involved in multi-stage bone grafting procedures and associated costs. While most bones grafting materials demonstrate osteoconductivity to regenerate bone, many suffer from poor mechanical properties, necessitating the use of ancillary fixation or containment devices to prevent graft migration and ingrowth of fibrous tissue that impedes bone regeneration and remodeling.

SOLUTION

Researchers at LaunchPad Medical are exploring a novel technology, Tetranite®, for bone grafting applications. Tetranite is an injectable, synthetic, wet-field bioresorbable biomaterial which can create a strong load-bearing bond between wet bone tissue and metals. The material is chemically and structurally stable in a neutral pH aqueous environment and is degraded and resorbed in vivo without the loss of bond to bone, resulting in continuous bone deposition to exposed surfaces.

COMPETITIVE ADVANTAGE

The unique hard-setting and adhesive properties of Tetranite enable it to conform and fixate to complex, open-walled, horizontal, and vertical defect sites. Given these unique properties, the material is predicted to eliminate the need for ancillary or graft containment devices currently required to support the existing bone graft. In addition, Tetranite enables immediate placement of implants simultaneous to the bone augmentation procedure, simplifying the bone grafting procedure. The reduction in surgical intervention and costs are expected to enable prosthetics to more widely benefit patients.

ITP SUPPORT

The work supported by the ITP program will prepare for the pivotal animal studies to assess the optimal Tetranite formulation for bone regeneration. The data from this investigation will better characterize the temporal formation of bone and resorption of the Tetranite graft material.

CLINICAL TRANSLATION PATHWAY

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Optimization of a Novel Organic-Mineral Bone Adhesive for Dental Bone Grafting
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UNMET CLINICAL NEED

Based on market research conducted by RevBio, almost half the patients that seek a dental implant supported crown suffer from chronic edentulism and require extensive bone grafting to rebuild their alveolar ridge (Figure 1), and over 30% of the time, these grafting procedures achieve less than desired results and require some form of re-grafting (Figure 2) adding to the overall cost, treatment time, and morbidity for these patients.

A marketing survey was conducted with significant support from The Avenue to verify the need for a grafting product with the unique attributes of TN. Twelve key opinion leaders in the field of dentistry were interviewed using a scripted set of questions to guide the discussions. A follow-up online survey was also conducted to generate quantitative data to support the qualitative data collected in the interviews.

RESULTS

The bone graft biomaterials used in this study consist of four TN test groups, two market controls (a cartridge-based injectable putty type of bioactive glass (NovaBone, OsteoGraft Biomedical, Inc., Lubbock, TX), MC1, and demineralized freeze dried bone allograft (OraGraft®, LifeNet Health, Virginia Beach, VA)) used in conjunction with a resorbable membrane and fixation screws, MC2, and two negative controls (empty defect sites filled with a blood clot with and without membranes). BCM and BDC, respectively, which were randomly assigned for placement into each of the 40 rectangular defects. Overall, each graft material was placed in 5 defect sites as per the original pilot study design.

Figure 6: Surgical Defect Creation and Deposit of TN Bone Graft Formulation, consisting of TN1 (left), empty defect (center 1), TN1 (center 2), Allograft with membrane-MC2 (right)

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Figure 7: Ridge Area Maintenance of the Graft Materials relative to Time 0d (Time 0d is when the graft materials were implanted immediately following the defect creation)

Figure 8: Coronal Plane through site of deposit of TN3 material into fresh alveolus. 10 weeks post implantation.

1. Polarized low magnification (left), 2. Bright field low magnification (center), 3. Bright field high magnification (right)

The architecture shown in the bright field image (center) and the orientation of collagen fibers in the polarized light image (right) indicate new bone that has been deposited as a replacement for the TN3 material in the area of deposition. The highlighted details show the only remaining TN3 material in the high magnification image (right), the remaining material having turned over to newly deposited bundle bone. No significant volumetric change occurred throughout the process.

Figure 9: Final Product Kit and Packaging

MANUFACTURING

RevBio has developed a pilot product kit representative of the anticipated commercial system which contains a sealed mixing bowl containing TN, a pre-filled syringe containing water to mix the adhesive, a grafting spatula, and an open bone delivery tray which is assembled, sealed and sterilized within a blister tray assembly (Figure 9). The delivery syringe is an off-the-shelf commercial system, which allows the TN material to be dispensed with control to the defect site.

Figure 10: Qualitative assessment of pore size porosity using uCT

The company has developed a lot release protocol which is conducted to characterize the physicochemical and mechanical properties of TN bone graft. A key parameter include compression strength, phase composition, echographic, and porosity as exhibited in Figure 10 using uCT.

REGULATORY PATHWAY

FDA previously designated TN as a device when used in conjunction with dental and orthopedic fixation devices. In January, 2020, the Company filed a Pre-Request for Designation (Pre-RFD) with the FDA Office for Combination Products (OCP) to address the stand-alone use of TN as a bone graft. The application has taken more than 230 days with the FDA reviewers citing delays due to the COVID-19 crisis.

Since the initiation of this product development effort significant progress has been made. In December 2020, RevBio will initiate its pivotal study, over 20 centers, to be conducted in volume (Figure 11). The results of this study will be used to prepare an Investigational Device Exemption (IDE) application for the FDA. Based on the Pre-RFD review, either a 510(k) route, a De Novo device, or a De Novo approval will likely result in the commercialization of this product.

REFERENCES

1. This data is based on results from a company survey consisting of 220 self-identified dental implant specialists (2019).
5. This project was made possible by a grant from the Michigan-Pittsburgh-Wyss Regenerative Medicine Resource Center and the NIH National Institute for Dental and Cranial Research (NIDCR), grant UH2DK095105. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.