OBJECTIVE

The purpose of this report is to provide an interim update on post-operative imaging studies evaluating the in vivo absorption profile and bony replacement of composite interference screws made from osteoconductive ß–TCP (beta-TriCalcium Phosphate) and PLGA (poly (L-lactide, co-glycolide)).

The absorption profile for the ß–TCP/PLGA material has been observed in a pre-clinical canine model1. The goal of these post-market imaging studies is to observe absorption characteristics when used for graft fixation in human Anterior Cruciate Ligament (ACL) reconstruction surgery. The preliminary results of two ongoing studies are described in this report.

MATERIALS AND METHODS

Two imaging studies are in progress utilizing ß–TCP/PLGA interference screws (MILAGRO® Interference Screw, DePuy Mitek, Raynham, MA) for graft fixation in ACL reconstruction surgery. The preliminary results of two ongoing studies are described in this report.

The first study (A) prospectively images subjects with implanted screws used to fixate patellar bone-tendon-bone (BTB) autografts or Achilles tendon allografts. The goal of this study is to evaluate in vivo screw absorption and any surrounding tissue response. The surgeries are completed by a single surgeon. In the BTB cases, ß–TCP/PLGA interference screws are implanted in both the femoral and tibial tunnels. The Achilles grafts are fixated with these screws only in the femoral tunnel adjacent to the bone block, and the fixation on the tibial side used other implant devices. The study is designed to capture MRI images at approximately 6, 12 and 24 months, and CT images at 12 and 24 months post implantation (+/- 2 months). Approximately 17 subjects have been imaged and analyzed through 12 months.

The second study (B) prospectively utilizes CT imaging to evaluate the long-term absorption of ß–TCP/PLGA interference screws used to fixate patellar BTB autografts in 10 subjects. The surgeries are completed by a single surgeon, and 5 of these subjects have been imaged at approximately 36 months post implantation.

Images captured in both Study A and B are analyzed by a third-party radiologist evaluating implant absorption, bony replacement and surrounding tissue response.
PRELIMINARY RESULTS – STUDIES A & B

For Study A, MRI was performed on 29 subjects (total of 53 interference screws) approximately 6 months post implantation (Figure 1a, b). All screws were visible and found to be intact. None of the following was observed: mass-like foreign body reactions, unexplained effusions, mechanical failure, lack of bone plug healing, lymphadenopathy, gross tunnel widening or gross osteolysis. Minor findings were present in a small number of subjects, including mild bone marrow edema-like signal, slight tunnel widening, and fluid signal in the soft tissues. These minor findings were not clinically or radiologically concerning but will be re-evaluated at future time points. Eleven of these 29 subjects had joint effusions, although these subjects had concomitant meniscal tears and/or significant chondral loss, which are likely sources for effusion.

Seventeen of these 29 subjects (total of 30 interference screws) have been evaluated with MRI and CT scans approximately 12 months post implantation (Figure 1c, d). Overall, the screws demonstrated some decrease in density and occasional fragmentation at this time point, suggesting preliminary absorption of β-TCP accompanied by polymer mass loss (Figure 2a-c). There was no observed progression of the minor findings from 6 to 12 months, and improvements were noted in several subjects, suggesting the initial signal changes were likely post-operative in origin. In three subjects, small fluid-filled collections were noted within the tendon graft and surrounding adjacent bone, but these were not likely specific to the screw implant. These minor findings will be re-assessed with imaging at later time points to more reliably assess any potential significance. None of these findings were considered clinically or radiologically concerning at this time point.

Figure 1a-d (Study A): MRI of Femoral Screw, 6 & 12 months. Sagittal T1-weighted (a, c) and T2-weighted with fat saturation (b, d) images at 6 (top row) & 12 months (bottom row) from the same subject with implanted Achilles allograft. Images demonstrate an intact screw with normal adjacent bone and soft tissues. A normal graft is noted posterior to the screw. Abnormal high T2-signal within the tibia (b) represents edema and/or granulation tissue from healing impaction fracture at 6 months from the original injury. This was resolved by 12 months (d).
Study B has imaged 5 subjects (total of 10 interference screws) with CT at approximately the 36-month time point. No residual screw material was observed, suggesting complete absorption of the β–TCP/PLGA material (trace amounts of non-mineralized polymer could still be present, but not specifically identifiable with CT). The screw site appears to have completely filled in with ossified tissue with similar appearance and density to the surrounding trabecular bone, suggesting bony replacement (Figures 3a-c and 4a-c). Additional subjects will be imaged at this time point.

**DISCUSSION**

The interference screws referenced in these studies consist of a homogeneous mixture of 30% β–TCP and 70% PLGA by weight. β–TCP is a well-known osteoconductive bioceramic often used in bone-void filling applications. Previously published imaging studies using β–TCP/polymeric interference screws have demonstrated various levels of ossification, and in some instances complete ossification at the screw site.

PLGA is a co-polymer consisting of 85 mole % L-lactide and 15 mole % glycolide. Poly-glycolide is typically a faster resorbing polymer than poly-L-lactide (PLLA). The addition of glycolide also disrupts the crystalline structure of PLLA, contributing to faster absorption characteristics of the co-polymer. Interference screws made of pure PLLA have been observed to take four years or longer to absorb with little or no evidence of ossification at the implant site. The PLGA co-polymer may allow for faster absorption of the screw and earlier bony replacement at the implant site.

Poandl T., et al. utilized a canine model to compare the in vivo absorption profiles of rods made of β–TCP/PLGA and pure PLLA. The rods were implanted in the femur and assessed at 3, 10, 18 and 24 months postoperatively. Histologic samples showed negligible absorption in either material at 10 months. However, marked absorption and bony replacement of the β–TCP/PLGA implants was observed between 18 and 24 months, while the PLLA rods remained largely intact at these later time points (Figure 6).
DISCUSSION CONTINUED

In Study A, the implanted β–TCP/PLGA interference screws appear intact via MRI and CT imaging at 6 and 12 months. These findings are consistent with the histological results from the canine study at these early time points. In Study B, no residual screw material was observed in the CT images at 36 months, and the implant sites appear to have completely filled in with ossified tissue. This is earlier than that reported for β–TCP implants combined with the slower absorbing PLLA polymer. Further imaging analysis of subjects at the 24-months time point will provide a more complete comparison between the pre-clinical model and human subjects, giving additional insights into the absorption and bony replacement properties of β–TCP/PLGA implants.

In Study A, no major imaging findings such as mechanical failure or foreign body reaction have been observed at the 6 and 12 month time points. Minor findings were noted in a few patients, including mild edema-like signal and slight tunnel widening. These findings are consistent with previously published imaging studies. Lajtai et al. reported mild edema and fluid collections in an MRI series using absorbable polymer interference screws in a BTB application. These findings were shown to resolve over time with no adverse clinical impact. Tunnel widening has been previously reported using metallic, absorbable polymer and composite interference screws. Lind et al. utilized radiographs to compare the tibial tunnel widths of hamstring ACL reconstructions at 12-months post implantation with either metal or Hydroxyapatite/PLLA composite interference screws. At the location of the screw implant, widening was observed in both groups, but was statically smaller in the absorbable composite group. MRI findings in Study A are consistent with observations in previously published reports, and will be re-assessed with imaging at later time points.

CONCLUSION

The MRI and CT Imaging studies to date are consistent with pre-clinical observations (animal model) and previous publications. At 6 and 12 months, the β–TCP/PLGA screws are visible in a BTB ACL application, and the device appears to be absorbed with observed bony replacement by 36 months. Continued follow-up at both the 24 and 36 month time points should yield a more specific absorption profile.

Figure 4a-c (Study B): 36 Month Sagittal (a) and Axial (b, c) CT images of a BTB subject with implanted screws on both the femoral and tibial side. Images show an intact bone plug, no observed polymer remnants, and filling of the implant site with dense, ossified tissue (black arrow). Dashed lines in sagittal image (a) mark locations for axial images (b,c).

Figure 5: Axial CT image of a BTB ACL reconstruction approximately 7 years post implantation with a PLLA screw. Screw appears to be absorbed and there is a lack of bony replacement in the implant profile (black arrow). Image provided by Dr. Alan Barber, Plano, TX.

Figure 6: Histologic samples from a canine femoral rod mode. Implanted rods consisting of β-TCP/PLGA show marked absorption and bony replacement between 18 and 24 months. Rods consisting of PLLA show negligible absorption at 24 months.

References