INTRODUCTION: Xenograft ACL reconstruction previously met with failure due to glutaraldehyde synoviitis, abrasion, poor fixation and immunologic rejection. Studies by Stone and Galili have shown that treatment of porcine tissues with alpha-galactosidase reduces immunologic recognition of the grafts preventing immune mediated rejection and destruction of the graft [1,2]. Pre-implantation biomechanical properties of treated porcine bone-patellar tendon-bone grafts matched human controls, and tests for biocompatibility and sterility met FDA guidance. Primate studies with treated porcine grafts demonstrated graft to host integration and gradual graft remodeling assessed at two, six and twelve months. This study is the first human clinical evaluation of ACL reconstruction with a porcine xenograft for the purpose of evaluating the safety and technical feasibility of the device.

METHODS: This was an FDA and IRB approved pilot clinical investigation in 10 human patients requiring ACL reconstruction. Porcine bone-patellar tendon-bone grafts were processed prior to implantation using recombinant alpha-galactosidase enzyme, low-level glutaraldehyde and terminally sterilized with 17.8 kGy electron beam irradiation. All patients received the porcine xenograft. The patient population was extremely athletic with mean age of 41 years (range 21-51) and distributed to seven males and three females. Fifty percent presented with complex chronic etiologies (injury to surgery >3 months). Previous surgeries to the affected/operative knees included: two ACL revisions; one ACL repair and three medial meniscal repairs. Three patients had previous ACL surgery of the contralateral knee. Study endpoints were effusion and knee stability as assessed by the principal investigator and an outside orthopaedic surgeon, MRI and serum antibody levels. Secondary endpoints included subjective measurements of activity level, pain and quality of life.

RESULTS: The device and surgery were well tolerated by all patients. Intra-operative surgical and technical feasibility objectives were met with device handling comparable to human patellar-tendon allografts. Six of ten subjects presented with grafts meeting effusion and laxity requirements at 12-months post-operatively. One of these six patients presented with activity-related variable effusion. In the course of the study, four subjects experienced non-operative related adverse effects: two subjects suffered sports-related trauma and graft rupture; and two subjects presented with laxity attributed to surgical/technical errors. These porcine grafts was eliminated by alpha-galactosidase and low-level glutaraldehyde treatments. Graft histopathology and resolving anti-pig antibody titers suggest a host remodeling and replacement of the implanted pig tendon device. Achievement of study endpoints after twelve-months supports the safety of the porcine xenograft device. A prospective double blind trial controlled against allograft is planned to evaluate the long-term efficacy of the device for ACL reconstruction.

DISCUSSION: Immunological rejection of these porcine grafts was eliminated by alpha-galactosidase and low-level glutaraldehyde treatments. Graft histopathology and resolving anti-pig antibody titers suggest a host remodeling and replacement of the implanted pig tendon device. Achievement of study endpoints after twelve-months supports the safety of the porcine xenograft device. A prospective double blind trial controlled against allograft is planned to evaluate the long-term efficacy of the device for ACL reconstruction.

REFERENCES:

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