

Summary of Clinical Research Involving Cayenne Medical Inc. Products

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At Cayenne Medical, we are committed to proper scientific investigation of the potential clinical benefits of using our devices. We are pleased to have multiple studies in clinically relevant areas currently underway by independent researchers, at highly reputable institutions in the U.S. and Internationally. Out of respect for the integrity of the scientific process, we will not cite specific authors until the studies have been published in peer-reviewed journals, presented at professional meetings, or until the author gives us permission. In the following sections, I will outline for you our published or presented research specific to Cayenne products, present selected topics on relevant subjects relating to clinical procedures, and give a brief overview of planned studies and questions to be answered for the remainder of 2013. Additionally, I will outline the other available forms of clinical material, such as White Papers. This summary is meant to be a concise review of the available research but we strongly encourage interested readers to consult the original source documents whenever possible. Many published studies and White Papers are available for download from our website or are available upon request from your Cayenne Medical technical representative.

New Publications and Presentations: Superior Tibial and Femoral Fixation; Outstanding Clinical Outcomes of AperFix[®] ACL Reconstruction; Biomechanical Equivalence to Native PCL

Aga, C. et al: "Biomechanical Comparison of Interference Screws and Combination Screw and Sheath Devices for Soft Tissue Anterior Cruciate Ligament Reconstruction on the Tibial Side" *Am J Sports Med* 41(4): 841-848, 2013.

- Non-sponsored study performed at Steadman Philippon Research Institute
- Cayenne AperFix tibial fixation performed best-in-class in all categories

TABLE 2
Biomechanical Properties of Tibial Soft Tissue Fixation Devices^a

Device	Cyclic Displacement, mm	Ultimate Failure, N	Displacement at Failure, mm	Load at 3-mm Displacement, mm	Pull-Out Stiffness, N/mm	Energy at Ultimate Failure, J
Bio-Interference Screw ^b	1.61 ± 0.22	973.3 ± 95.82	5.31 ± 0.51	703.8 ± 74.50	343.0 ± 46.43	2.92 ± 0.51
BIOSURE PK ^b	1.72 ± 0.29	990.8 ± 182.1	5.65 ± 1.35	721.2 ± 92.45	352.3 ± 42.73	3.45 ± 1.40
RCI Screw ^b	1.97 ± 0.39	817.7 ± 114.0	4.80 ± 2.07	676.3 ± 157.2	384.3 ± 105.2	4.80 ± 2.07
AperFix II ^c	1.58 ± 0.21	1122 ± 182.9	5.43 ± 1.54	782.8 ± 171.0	366.4 ± 40.76	3.66 ± 1.05
BIOSURE SYNC ^c	1.92 ± 0.59	829.5 ± 172.4	6.54 ± 2.90	632.0 ± 154.9	326.9 ± 74.51	6.54 ± 2.90
ExoShape ^c	1.68 ± 0.30	814.7 ± 178.8	5.27 ± 1.25	663.8 ± 125.5	342.3 ± 51.47	2.80 ± 1.10
GraftBolt ^c	1.38 ± 0.27	1136 ± 115.6	5.98 ± 1.47	767.6 ± 146.0	402.3 ± 58.89	4.00 ± 1.47
INTRAFIX ^c	1.63 ± 0.15	1127 ± 155.0	6.43 ± 1.24	709.9 ± 118.4	372.5 ± 50.02	4.38 ± 1.64

^aData are shown as means ± standard deviations.

^bScrew device.

^cCombination device (screw and sheath).

Ehrensberger, M., Bisson, L., et al: "Biomechanical Comparison of Femoral Fixation Devices for Anterior Cruciate Ligament Reconstruction Using A Novel Testing Method" *Clinical Biomechanics* 28(2): 193-198, 2013.

- Non-sponsored study performed at State University of New York at Buffalo
- Novel testing apparatus allowed isolation of individual fixation elements, such as implant vs graft elongation
- Outcomes included tendon elongation, anchor displacement, stiffness, maximum load, yield load, and load at 5mm of anchor displacement
- Outstanding biomechanical results found for all tested parameters
- Zero graft slippage in femur, indicating that strong aperture fixation is present with the AperFix device

Uribe, J. et al: "Two Year Outcome With The AperFix System For ACL Reconstruction" *Orthopedics* 36(2) 159-164, 2013.

- 185 knees studied for KT-1000 arthrometry and functional outcomes after hybrid soft-tissue ACL reconstruction using AperFix femoral and tibial fixation
- Average KT-1000 side-to-side difference was 0.4mm, outstanding compared to other methods in the published literature
- Lysholm, Tegner, and patient activity scores showed significant improvements compared to preoperative condition, and all scores are comparable to the best scores published for BTB autograft ACL reconstruction

Mutnal, A., Leo, B., et al: "Biomechanical Analysis of Posterior Cruciate Ligament Reconstruction Using Aperture Femoral Fixation" *Presented at American Academy of Orthopaedic Surgeons 2013 Annual Meeting and Submitted for Publication to Arthroscopy Journal.*

- Non-sponsored study performed at the Cleveland Clinic
- Single bundle PCL reconstruction with the AperFix femoral and tibial devices resulted in a kinematically normal knee compared to the intact PCL

Biomechanical Testing of the Femoral AperFix® Device Shows Ultimate Load To Failure Equal To Cross-Pin Fixation for ACL Reconstruction

This study is available as a White Paper and shows that the time-zero strength of fixation of the femoral AperFix device is equal to two of the most commonly used femoral soft-tissue fixation devices, and stronger than interference screw fixation.

- Abell, B., and Wenger, K.: "Biomechanical comparison of femoral fixation devices in soft-tissue ACL reconstructions" *Cayenne Medical Inc., White Paper*

Ultimate load to failure (N)	
AperFix®	1479 +/- 261
BioTransFix®	1472 +/- 244
Endobutton®	1311 +/- 178
Biointerference screw	935 +/- 147

Premarket scientific studies of basic principles highlight the benefits of aperture fixation, shorter graft length, and reproduction of the native helical ACL architecture to give the best possible ACL construct. The Cayenne AperFix® implants allow the surgeon to incorporate these best practices into the reconstruction.

- **Animal studies show that shorter graft intra-osseous lengths are equally effective in terms of biomechanical testing compared to longer intra-osseous lengths**
 - **Healing takes place principally at the aperture of the tunnel where the tendon is firmly compressed against bone**
 - **An implant that allows aperture fixation at the tunnel openings will give the shortest intra-articular graft length**
 - **The shortest intra-articular graft length yields stiffness closest to the native ACL**
 - **A double-bundle helical graft architecture closely replicates the native ACL in terms of mechanical testing**
- Brown CH Jr, Sklar JH: Endoscopic anterior cruciate ligament reconstruction using quadrupled hamstring tendons and Endobutton femoral fixation. *Tech Orthop* 13: 281–298, 1998
 - Hoher J, Livesay GA, Ma CB, et al: Hamstring graft motion in the femoral bone tunnel when using titanium button/polyester tape fixation. *Knee Surg Sports Traumatol Arthrosc* 7: 215–219, 1999
 - Hoher J, Scheffler SU, Withrow JD, et al: Mechanical behavior of two hamstring graft constructs for reconstruction of the anterior cruciate ligament. *J Orthop Res* 18: 456–461, 2000
 - Rowden NJ, Sher D, Rogers GJ, et al: Anterior cruciate ligament graft fixation. Initial comparison of patellar tendon and semitendinosus au- tografts in young fresh cadavers. *Am J Sports Med* 25: 472–478, 1997
 - Yagi, M., Wong, E.K., Kanamori, A., Debski, R.E., Fu, F.H., Woo, S. L-Y.: "Biomechanical Analysis of an Anatomic Anterior Cruciate Ligament Reconstruction" *Am J Sports Med.* 2002; 30(5): 660-666.

- Yamazaki, S., Yasuda, K., Tomita, F., Minami, A., Tohyama, H.: “The effect of intraosseous graft length on tendon-bone healing in anterior cruciate ligament reconstruction using flexor tendon” *Knee Surg Sports Traumatol Arthrosc* 2006; 14:1086–1093.
- Zantop, T., Ferretti, M., Bell, K.M., Brucker, P.U., Gilbertson, L., and Fu, F.H.: “Effect of Tunnel-Graft Length on the Biomechanics of Anterior Cruciate Ligament_Reconstructed Knees: Intra-Articular Study in a Goat Model” *Am. J. Sports Med.* 2008; 36: 2158-2166.

Published biomechanical study shows that the single-tunnel double-bundle Cayenne AperFix® ACL reconstruction provides a closer approximation to intact knee kinematics than single-bundle reconstructions

This cadaveric biomechanical study compared the kinematics of four conditions: ① The intact knee, ② The ACL deficient knee, ③ Single-bundle reconstruction using quadrupled hamstring tendon, and ④ Single-tunnel double-bundle reconstruction using AperFix®

- **The single-tunnel-double-bundle anterior cruciate ligament reconstruction more closely restored the intact knee kinematics than the single-bundle anterior cruciate ligament reconstruction at low flexion angles (< or =30 degrees) under the anterior tibial load and simulated muscle load (P < .05). This double-bundle anterior cruciate ligament reconstruction using a single tunnel can better restore anterior tibial translations to the intact level compared with single-bundle anterior cruciate ligament reconstruction at low flexion angles.**
- **The AperFix® femoral and tibial implants allow the surgeon to rotate the graft bundles, resulting in a helical double-bundle construct that closely approximates the native ACL architecture**

- Gadikota, H.R., Seon, J.K., Kozanek, M., Oh, L.S., Gill, T.J., Montgomery, K.D., Li, G.: “Biomechanical Comparison of Single-Tunnel Double-Bundle and Single-Bundle Anterior Cruciate Ligament Reconstructions” *Am J Sports Med*, 2009 May;37(5):962-9.

Published clinical studies and white papers show outstanding near-term functional results, no tunnel widening, and highlight technical aspects of ACL reconstruction and revision with the AperFix® System

- **Significant improvements in Lysholm score compared to cross-pin fixation**
- **No tunnel widening**
- **Significant improvements in stability, IKDC score, single leg hop, surgical time**
- **Potential for differential bundle tensioning of the anteromedial and posterolateral bundles**
- **Technical note highlights straightforward steps in implant removal for revision**

- Burke, Robert: “Tunnel widening comparison for AperFix vs Cross Pin”
- *Cayenne Medical Inc. White Paper*
- Connor, Geoff: “Outcomes in ACL Reconstruction Using the AperFix System”
- *Cayenne Medical Inc. White Paper*
- Cooper, W., Machen, M.S., Nelson, J., Owens, B.D.: “Anterior Cruciate Ligament Revision of a Relatively New Implant System” *Orthopedics*, 2009 May; 32(5): 326-328.
- Schachter, A.K., and Montgomery, K.D.: “Single-Tunnel Double-Bundle Anterior Cruciate Ligament Reconstruction” *Tech Knee Surg*, 2009; 8(2) 110-114.
- Uzumcugil, O., Dogan, A., Dalyaman, E., Yalcinkaya, M., Akman, E., Ozturkmen, Y., Caniklioglu, M.: “AperFix versus TransFix in Reconstruction of Anterior Cruciate Ligament”
- *J Knee Surg* 2010; 23(3):29-35.

Ongoing: prospective arthrometry and functional outcomes of AperFix[®] ACL reconstruction comparing transtibial drilling to anteromedial portal drilling

- **Prospective outcomes study from Lake Success, NY, and San Diego, CA**
- **Submitting for presentation at 2014 American Academy of Orthopaedic Surgeons Annual Meeting**

Published technical notes and case series highlight the ease of use and reproducibility of the Cayenne AperFix[®] femoral and tibial implants for single-tunnel double-bundle PCL reconstruction

- **Portal placement, tunnel placement, and surgical steps described in detail**
- **A method of differential tensioning of the anterolateral and posteromedial bundles is described utilizing a single-tunnel double-bundle technique**
 - Baker, C.L. Jr., and Baker, C.L. III: "Arthroscopic PCL reconstruction with a soft tissue system" *Orthopedics Today SuperSite* publication: <http://www.orthosupersite.com/view.aspx?rid=66151>
 - Uribe, J.W., Vargas, L., Leo, B.M.: "Arthroscopic PCL reconstruction with a novel all-inside femoral fixation device: a single-incision technique" *Orthopedics* 2010; 33(2):92-97.

Ongoing: biomechanical evaluation of transosseous equivalent rotator cuff repair

- **Cadaver biomechanical study underway in Birmingham, AL**
- **Testing scheduled for completion in July, 2013**