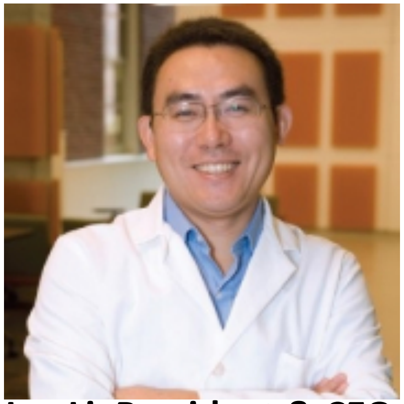
Better Life Through Innovation

FiberFIX™ Bioresorbable Implants

HA Nanofiber Reinforced Biocomposite

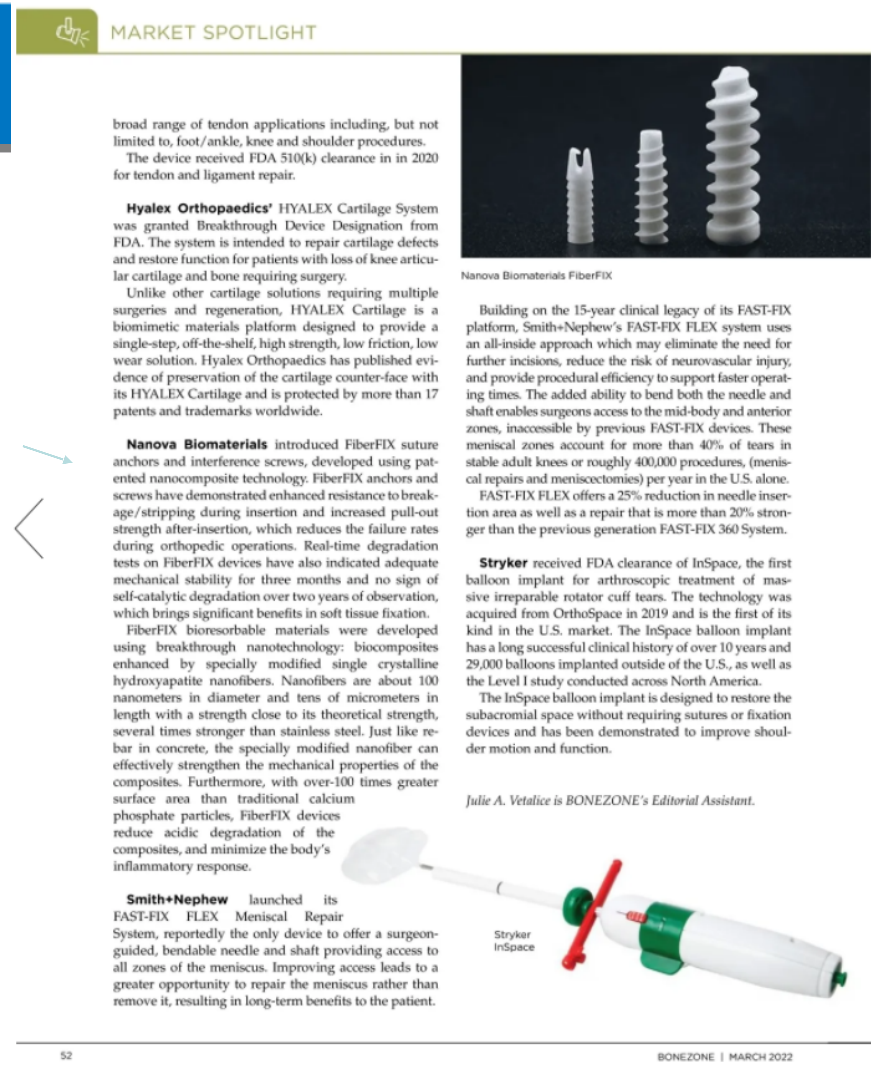
Richard Joseph Lebens PhD

Nanova Biomaterials Inc. and FiberFIX™



Hao Li, President & CEO

- A scientific and technological innovation enterprise that applies advanced biomaterial technology for medical devices.
- Focus on minimally invasive surgery (sports medicine/arthroscopy, laparoscopy) and medical cosmetology (oral, skin/wound), etc.
- Innovative and leading core technologies, including "polymer composites" and "low temperature plasma".



MARKET SPOTLIGHT

broad range of tendon applications including, but not limited to, foot/ankle, knee and shoulder procedures.

The device received FDA 510(k) clearance in in 2020 for tendon and ligament repair.

Hyalex Orthopaedics' HYALEX Cartilage System was granted Breakthrough Device Designation from FDA. The system is intended to repair cartilage defects and restore function for patients with loss of knee articular cartilage and bone requiring surgery.

Unlike other cartilage solutions requiring multiple surgeries and regeneration, HYALEX Cartilage is a biomimetic materials platform designed to provide a single-step, off-the-shelf, high strength, low friction, low wear solution. Hyalex Orthopaedics has published evidence of preservation of the cartilage counter-face with its HYALEX Cartilage and is protected by more than 17 patents and trademarks worldwide.

Nanova Biomaterials introduced FiberFIX suture anchors and interference screws, developed using patented nanocomposite technology. FiberFIX anchors and screws have demonstrated enhanced resistance to breakage/stripping during insertion and increased pull-out strength after-insertion, which reduces the failure rates during orthopedic operations. Real-time degradation tests on FiberFIX devices have also indicated adequate mechanical stability for three months and no sign of self-catalytic degradation over two years of observation, which brings significant benefits in soft tissue fixation.

FiberFIX bioresorbable materials were developed using breakthrough nanotechnology: biocomposites enhanced by specially modified single crystalline hydroxyapatite nanofibers. Nanofibers are about 100 nanometers in diameter and tens of micrometers in length with a strength close to its theoretical strength, several times stronger than stainless steel. Just like rebar in concrete, the specially modified nanofiber can effectively strengthen the mechanical properties of the composites. Furthermore, with over-100 times greater surface area than traditional calcium phosphate particles, FiberFIX devices reduce acidic degradation of the composites, and minimize the body's inflammatory response.

Smith+Nephew launched its FAST-FIX FLEX Meniscal Repair System, reportedly the only device to offer a surgeon-guided, bendable needle and shaft providing access to all zones of the meniscus. Improving access leads to a greater opportunity to repair the meniscus rather than remove it, resulting in long-term benefits to the patient.

Nanova Biomaterials FiberFIX

Building on the 15-year clinical legacy of its FAST-FIX platform, Smith+Nephew's FAST-FIX FLEX system uses an all-inside approach which may eliminate the need for further incisions, reduce the risk of neurovascular injury, and provide procedural efficiency to support faster operating times. The added ability to bend both the needle and shaft enables surgeons access to the mid-body and anterior zones, inaccessible by previous FAST-FIX devices. These meniscal zones account for more than 40% of tears in stable adult knees or roughly 400,000 procedures, (meniscal repairs and meniscectomies) per year in the U.S. alone.

FAST-FIX FLEX offers a 25% reduction in needle insertion area as well as a repair that is more than 20% stronger than the previous generation FAST-FIX 360 System.

Stryker received FDA clearance of InSpace, the first balloon implant for arthroscopic treatment of massive irreparable rotator cuff tears. The technology was acquired from OrthoSpace in 2019 and is the first of its kind in the U.S. market. The InSpace balloon implant has a long successful clinical history of over 10 years and 29,000 balloons implanted outside of the U.S., as well as the Level I study conducted across North America.

The InSpace balloon implant is designed to restore the subacromial space without requiring sutures or fixation devices and has been demonstrated to improve shoulder motion and function.

Julie A. Vetalice is BONEZONE's Editorial Assistant.

Stryker InSpace

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BONEZONE | MARCH 2022

Vetalice, Julie. "*Sports Medicine Companies and Products to Know*" BoneZone, vol. 21 no. 1 March 2022 p.52

Current Orthopedic Materials In Surgeons tool Bag for Soft Tissue Fixation

Why metal Implants?

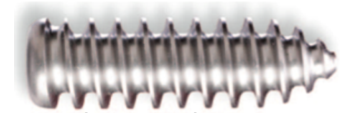
- Advantages: excellent mechanical properties and easy to be sterilized;
- Drawbacks: secondary surgery, MRI imaging artifact , and stress shielding.

Why Bioresorbable implants?

- Advantages: no secondary surgery, no load shielding for better tissue healing, and compatibility with MRI imaging;
- Drawbacks: reduced strength, and late term inflammatory response.

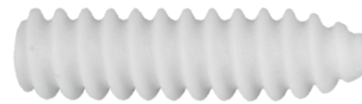
Why most use Biocomposite currently?

- Hydroxyapatite($Ca_{10}(PO_4)_6(OH)_2$) as main component of bone minerals
- Increased stiffness to match the stiffness of bone
- Buffer acidic byproducts from degradation[1]
- Incorporation of HA slows adverse degradation[2]
- Improved osteoconductivity[3]



Generation 1 (Metal)

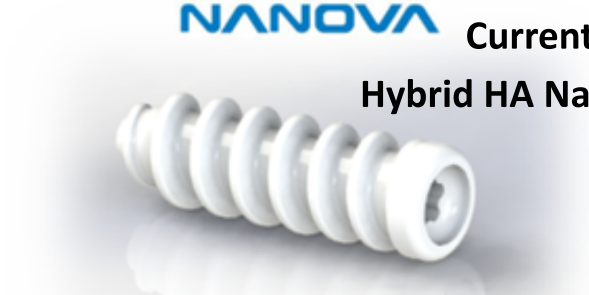
Generation 2 (Bioabsorbable polymer)



Generation 3 (Biocomposite)

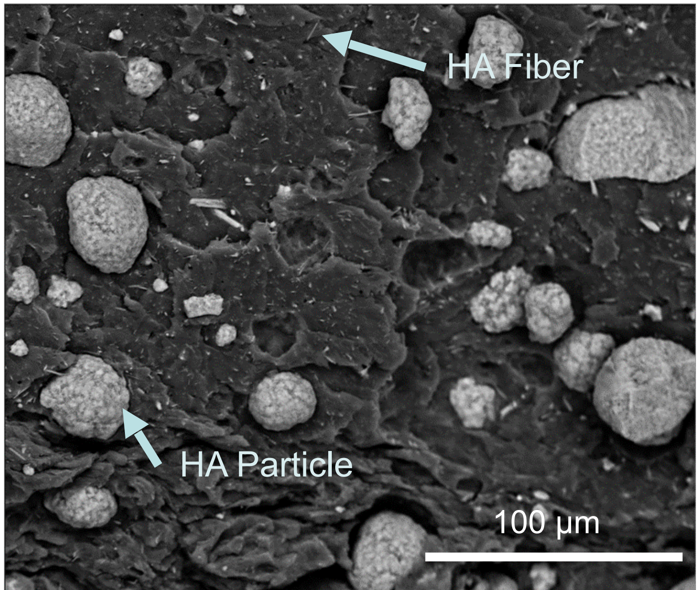
NANOVA **Current state of the Art:**

Hybrid HA Nanofiber Biocomposite

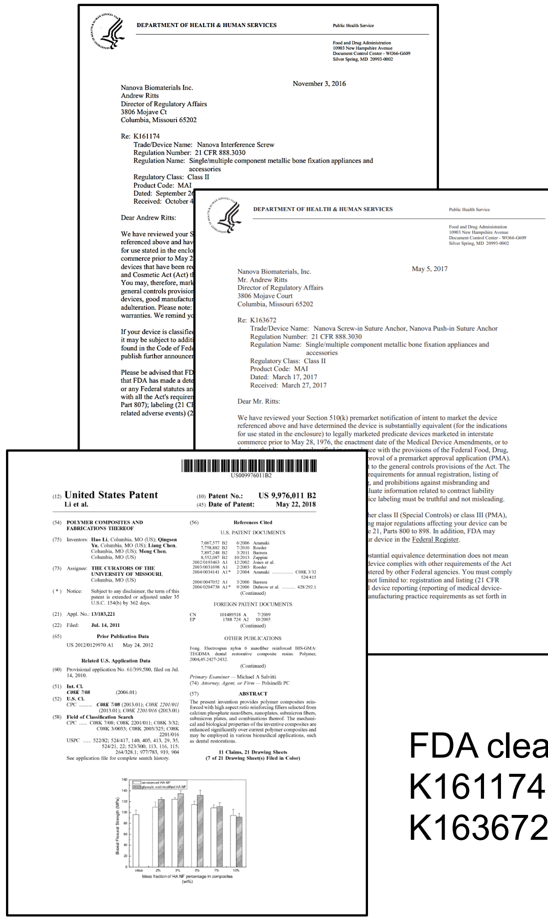


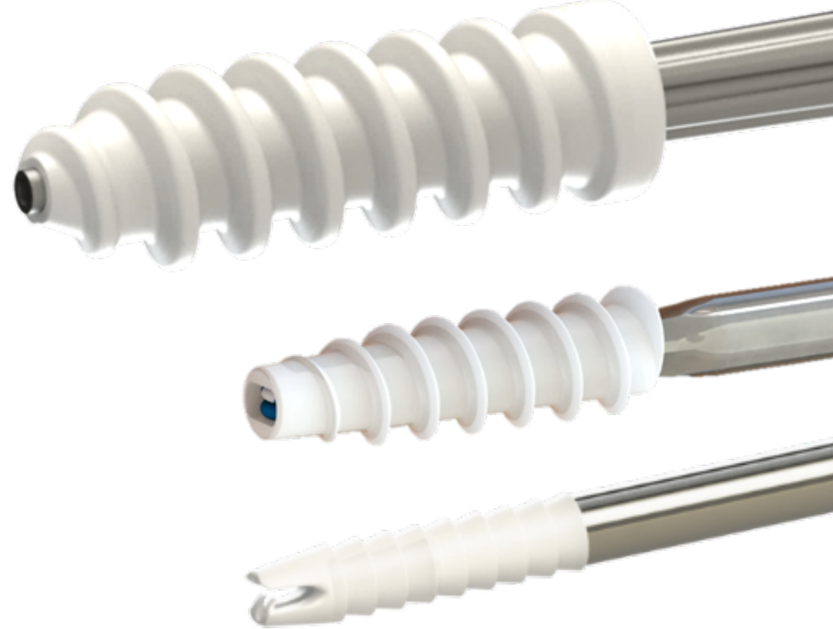
1. *Hunt et al. 2008*
2. *Hasegawa et al.2006*
3. *Hile et al. 2004, Tecklenberg et al. 2006*

Current state of the Art: HA Nanofiber Reinforced Biocomposites



Patented Material Technology (US20120129970A1)





Patented Pending design (63186473)

FDA cleared
K161174 Interference Screw &
K163672 Suture Anchor

HA Nanofibers's High Surface Area Enhances Inflammatory Buffer

PLLA device implanted in bone tissue

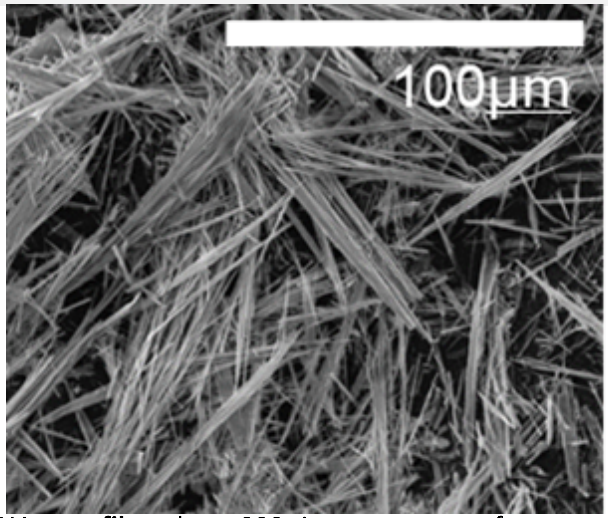
Superficial erosion occurs, and fragmentation is caused by the hydrolytic degradation process

Inflammatory response production of lactic acid and decrease in pH

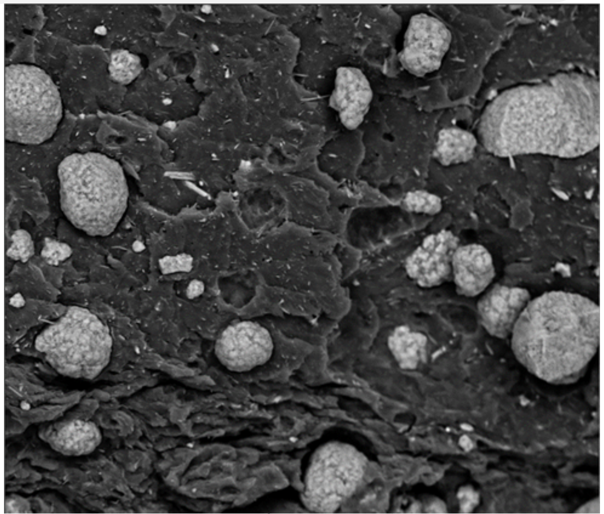
Material has been degraded and phagocytosed by inflammatory cells

- The hydrolytic degradation process induces a decrease in pH, which changes the inflammatory response from acute to chronic;
- Presence of calcium phosphate buffers inflammatory response;
- Buffer effect strongly correlated to surface area, HA fiber significantly increase surface area.

- The FiberFix™ composite has **37-45** times greater calcium phosphate surface area compared to commercial HA or TCP particle devices

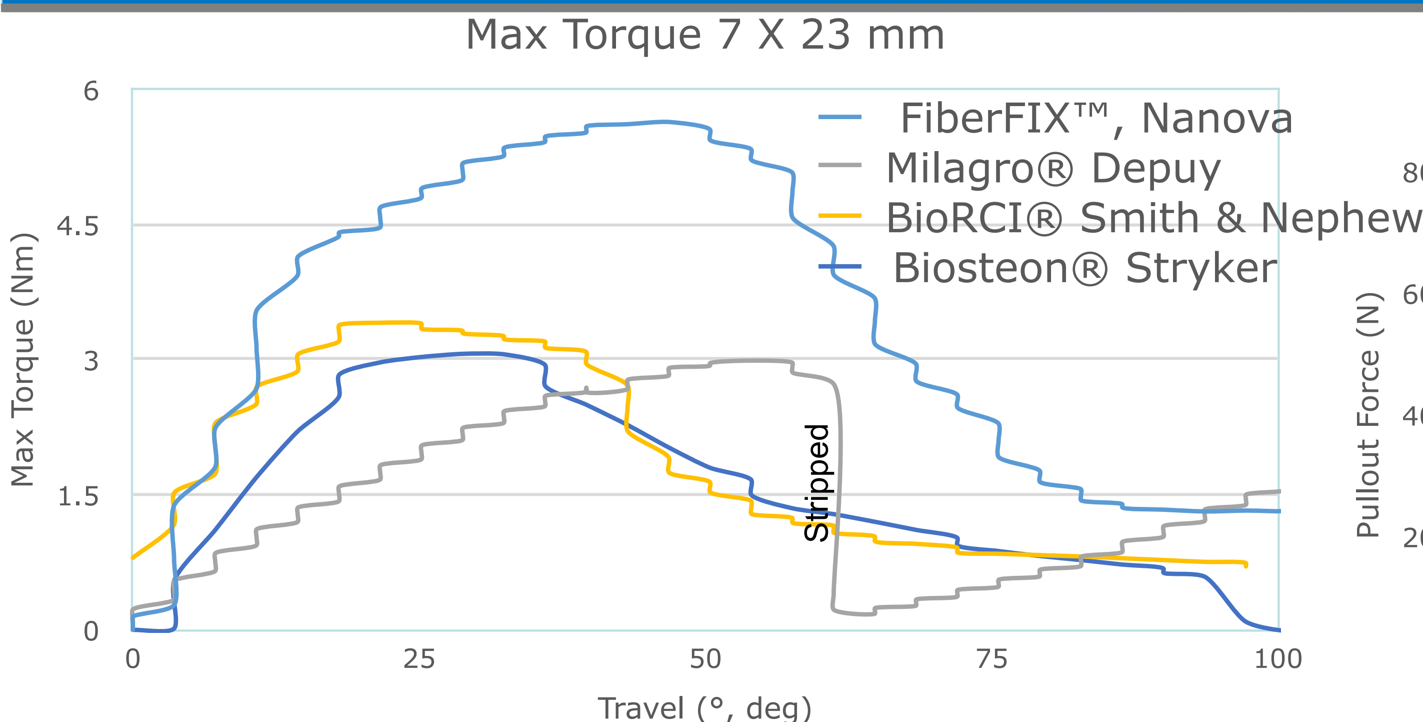


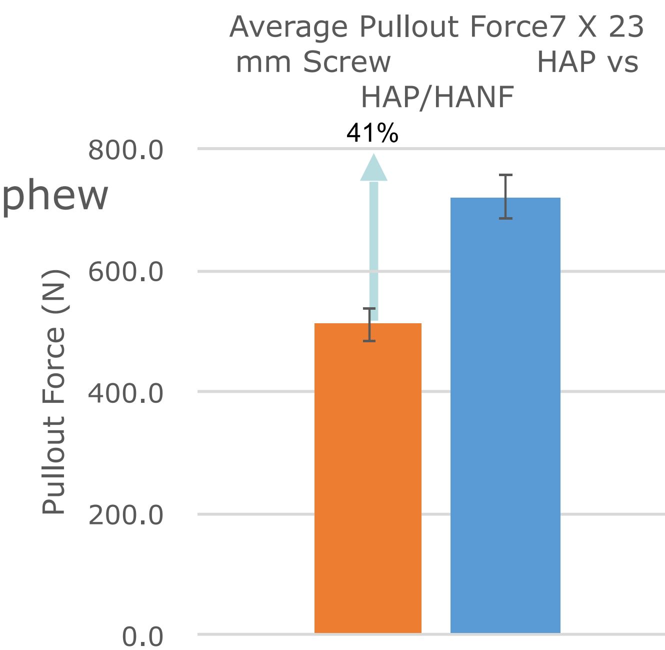
HA **nanofibers** have 222 times greater surface area compared to HA particle (~20µm) per gram



FiberFix™ Fracture surface SEM showing homogeneous distribution of HA

Nanova™ Hybrid HA Composite Devices Mechanical Enhancement: “Bend Before They Fracture”





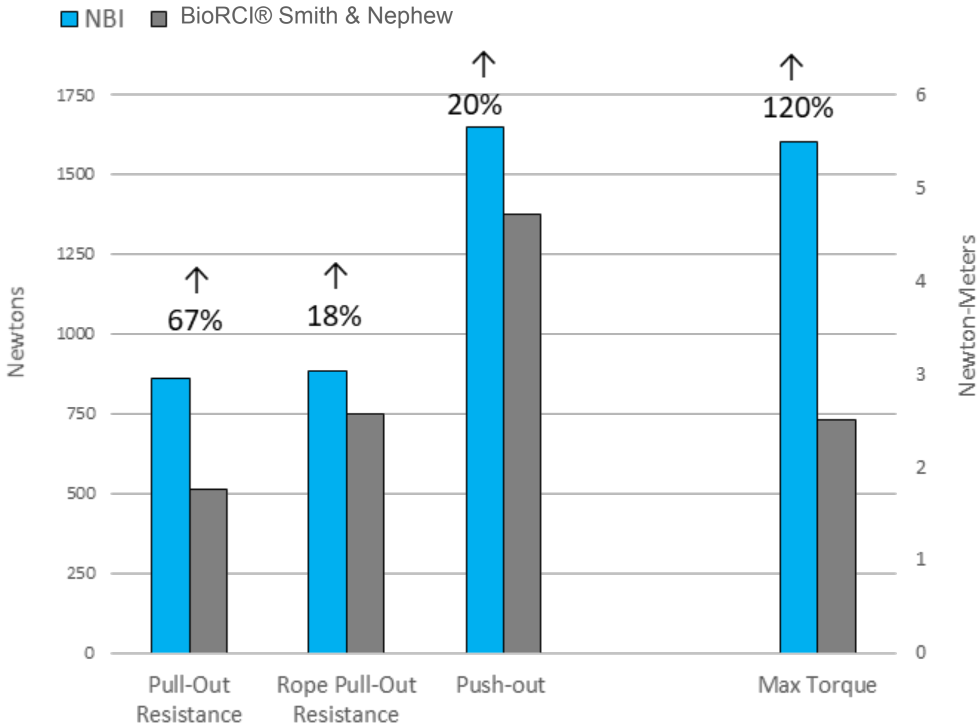
7 X 23 mm Pullout Force	
HAP	510.5 ± 28.5
HAP/HANF	720.7 ± 37.5

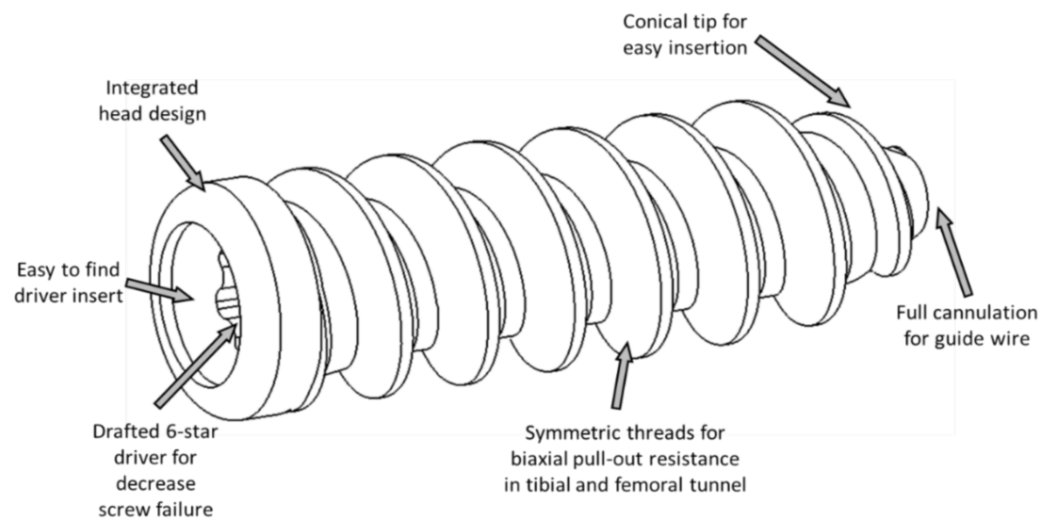
- 56% increase in max torque comparing to competitor 2
- Significant increase in toughness (area under the curve)

- 41% increase in strength compared to HA particles alone

FIberFix™ Interference Screw Design & Bench Testing

FiberFix™ Competitive Advantage

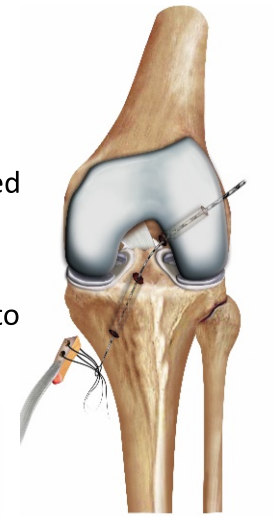




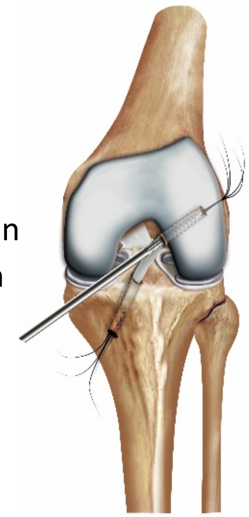
Data on file Nanova Biomaterials Inc, 7 X 23 mm interference screw submitted to FDA under FDA 510(k) K161174

Interference Screw Procedure

The knee is prepared for arthroscopic surgery using standard methods to place portals.

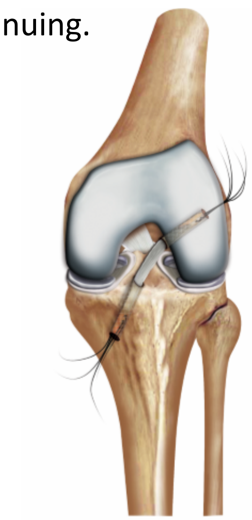


Once the tunnels have been created, use a passing suture to pass the graft into the joint through the tibial tunnel and then femoral tunnel. Maintain tension on the graft, and ensure correct placement of graft before continuing.

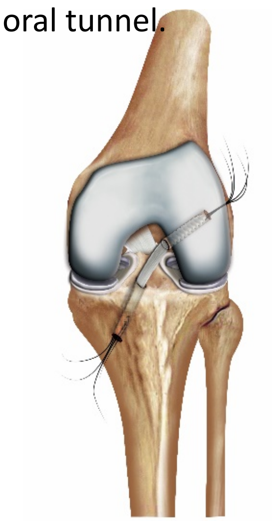


Maintaining tension on the graft, fix the femoral side of the graft with the interference screw in standard fashion (Figure 5). The screw should be advanced until the head is counter sunk slightly in the femoral tunnel.

A graft is obtained and prepared for reconstruction through standard procedures.

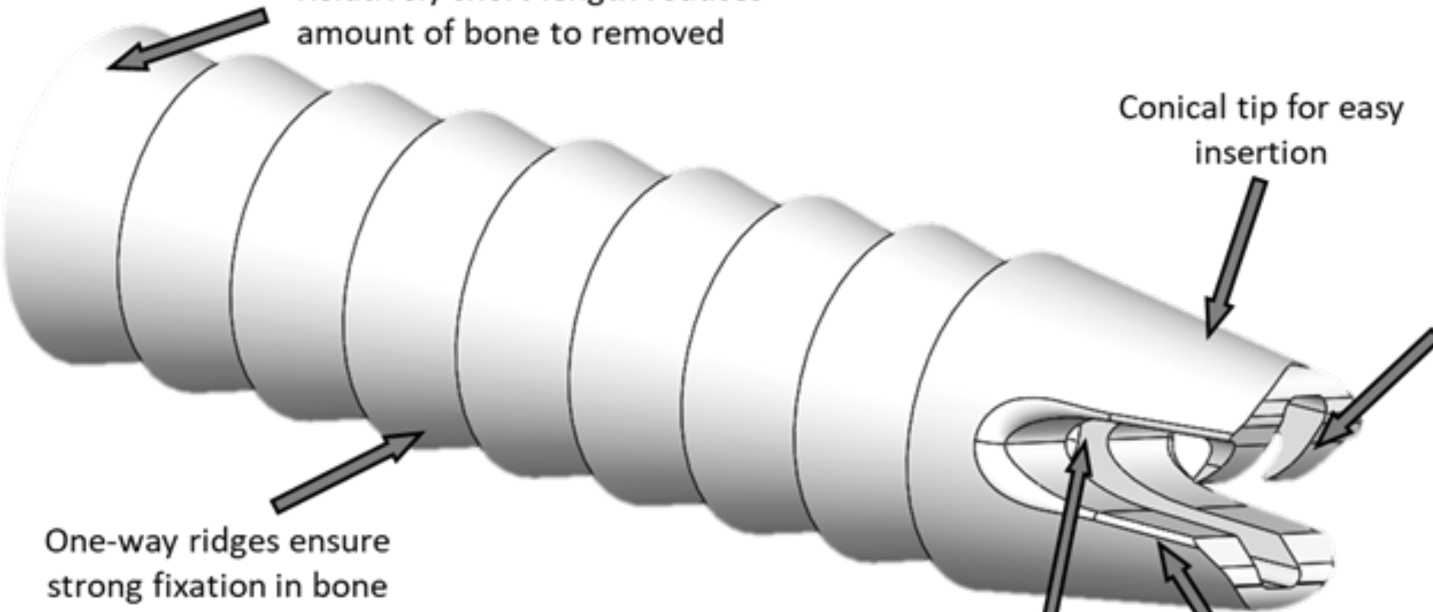


Place a guide wire in the femoral tunnel. If desired, the surgeon may tap over the guide wire to create a pre-threaded hole for the interference screw. Remove the tap and place the screw securely on the screw driver. Insert the interference screw over the guide wire and into the knee joint.



Ensure that graft tension is maintained during placement of the screw . Check that full extension of the knee is possible.

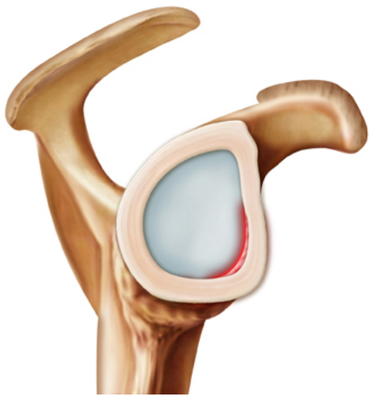
FiberFix™ Push-In Anchor Design



Knotless approach

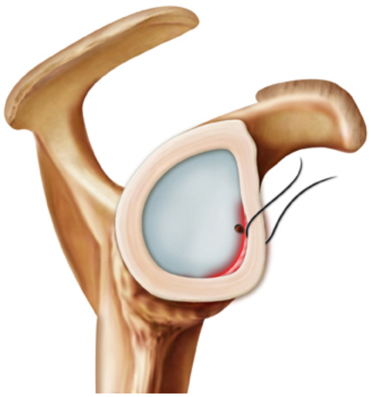
Push-in Technique for Glenoid Labral Repair

1



The shoulder is prepared for arthroscopic surgery using standard methods to place portals in typical locations.

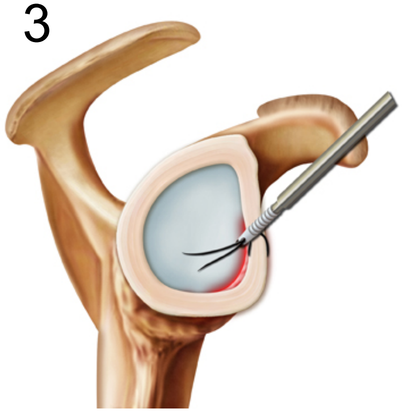
2



Place a suture through the labrum or capsule according to the surgeon's preference. Pull the two ends of the suture back out through the cannula to prevent loss of the suture.

Drill a pilot hole for the suture anchor to the proper depth, ensuring firm pressure on the guide to prevent slippage or rotation.

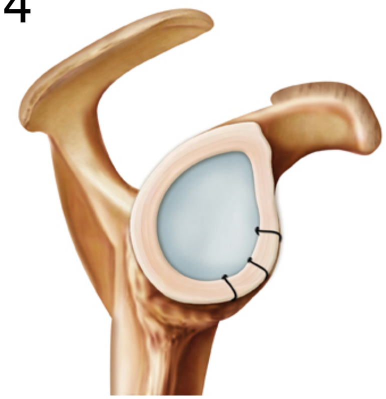
3



Clip the suture flush with the surface using a suture cutter. If additional fixation is needed, the pre-threaded suture may be passed through the soft tissue.

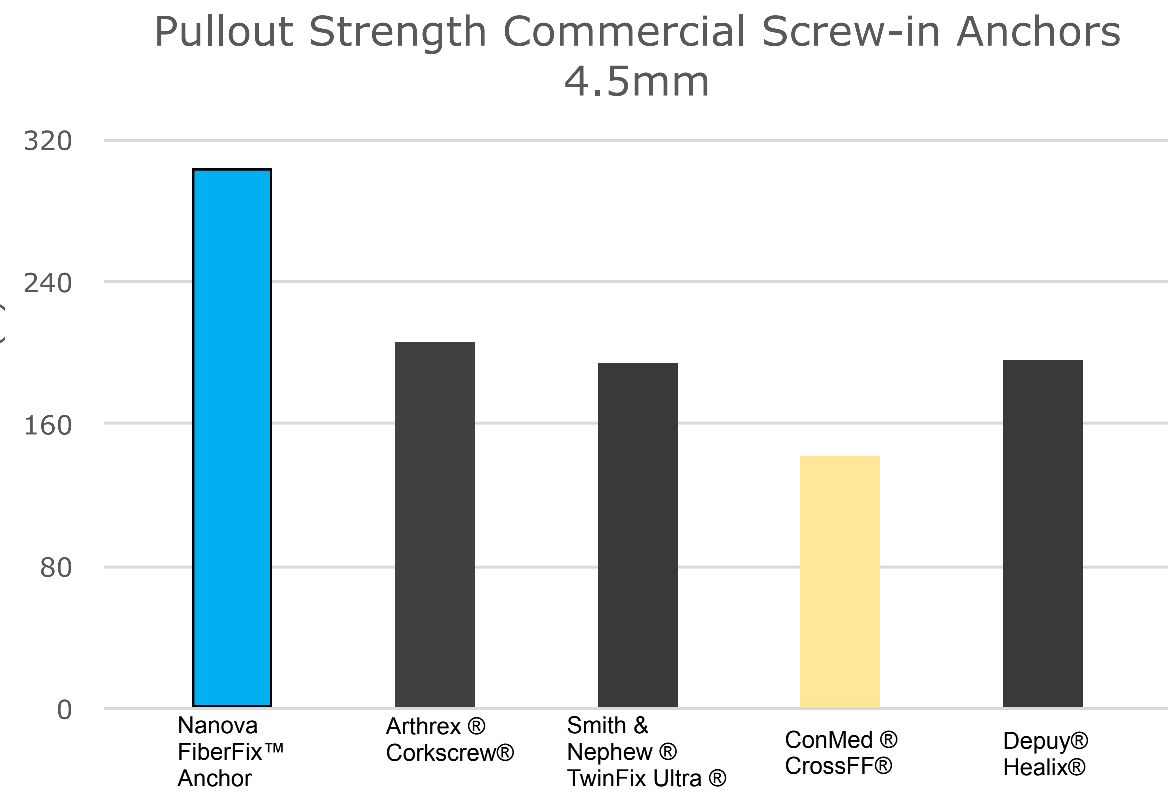
Repeat steps as deemed appropriate by the surgeon and the size of the injury in order to complete the repair

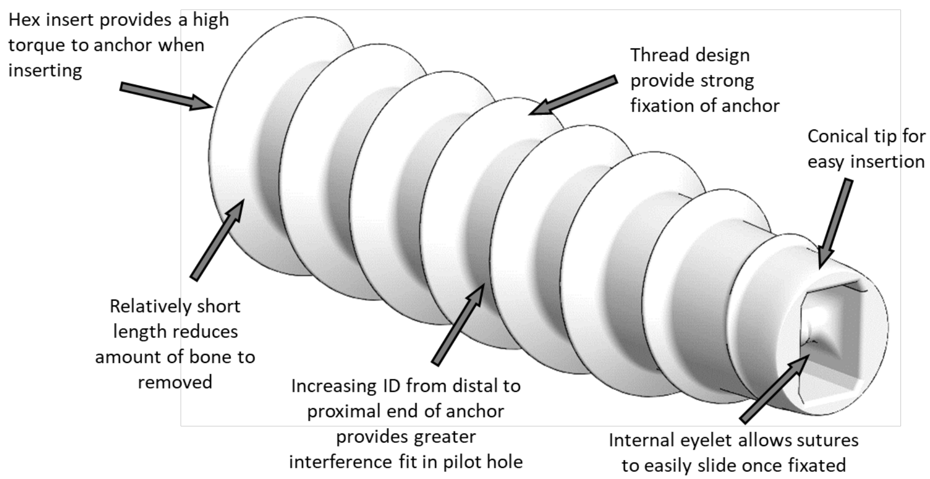
4



Capture the ends of the suture that was threaded around or through the labrum with the prongs of the suture anchor. Place the suture anchor and driver through the guide, taking care that the suture remains between the prongs.

FiberFIX™ Screw-in Anchor Design & Bench Testing





Data on file Nanova Biomaterials Inc, 4.5mm screw-in anchor submitted to FDA under FDA 510(k) K163672

Screw-in Anchor Procedure for Rotator Cuff Repair

The shoulder is prepared for arthroscopic surgery. Place portals in standard locations. The joint is examined, and the injury is prepared using an arthroscopic shaver and/or rasp

Prepare a pilot hole in the humerus by tapping the instrument with a mallet, ensuring that the punch is inserted to the laser line

Place a suture anchor and driver through the cannula and align with one of the pilot holes. Screw the anchor into the bone to the appropriate depth, ensuring that the anchor is flush or subflush with the bone.

Pass each strand of suture through the rotator cuff tendon according to the surgeon's preference (Figure 4).

Retrieve two corresponding ends of suture from the accessory portal and out of the cannula. Tie the sutures and shuttle the knot back into the shoulder. The tied suture should pull the tendon over the suture anchor, and the knot should sit as closely to the suture anchor as possible.

Declining Confidence in Absorbable Materials

Manufacturer	Product Name	Polymer (matrix)	%	Composite (fill)	%
	Material Composition				
Arthrex ®	Biocomposite Interference Screw	PLDLA (70/30)	70%	BCP (60HA/40β-TCP)	30%
Smith & Nephew®	BioRCI-HA ®	PLLA	75%	HA	25%
Smith & Nephew®	Biosure ®	PLGA (85/15)	65%	(57 $CaSO_4$/43 β-TCP)	35%
Stryker ®	Biosteon®	PLLA	75%	HA	25%
DePuy Mitek ®	Milagro®	PLGA (85/15)	70%	β-TCP	30%
DePuy Mitek ®	BioCryl®	PLLA	70%	β-TCP	30%
ConMed Linvatec ®	Matryx®	SR-PLDLA (96/4)	75%	β-TCP	25%
ArthroCare ®	BiLok ®	PLLA	75%	β-TCP	25%
Nanova ™	FiberFix ™	PLDLA (70/30)	75%	HA	25%

Slower degradation

Milagro® Screw (PLGA)

FIBERFIX™ (PLDLA)

BioRCI-HA® Screw (PLLA)

Negative studies have reduced the appeal of traditional absorbables

NANOVA

Nanova HA/PLA Composite Bone Implantation Histopathology and Inherent Viscosity Study

Conclusions:

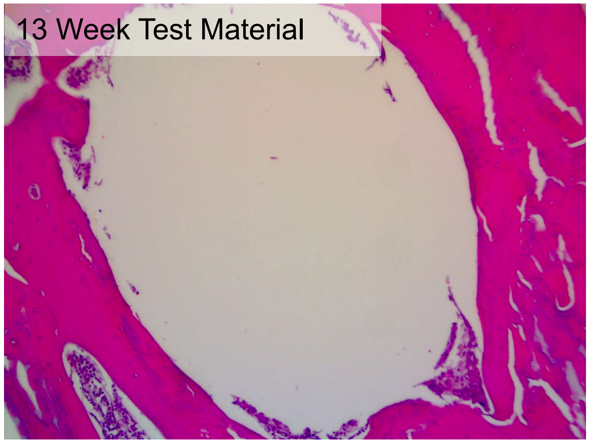
Histology

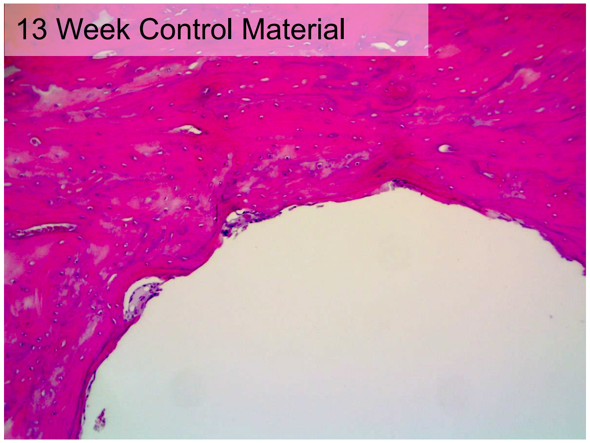
- Similar new bone formation and resorption/remodeling between test and control sites
- No inflammation at test and control sites
- Test article exhibited no potential to induce local toxic effects in the skeletal tissues

Inherent Viscosity

- FiberFx™ with PLDLA matrix demonstrates faster degradation compared to BioRCI® (PLLA), but slower compared to Milagro® (PLGA)

	T0	T4	T8	T12	T16
MILAGRO (PLGA)	2.15	1.44	1.27	1.10	1.03
FIBERFIX (PLDLA)	2.7	1.72	1.71	1.57	1.34
BIORCI (PLLA)	2.65	2.38	2.75	2.57	2.22
	Inherent Viscosity				

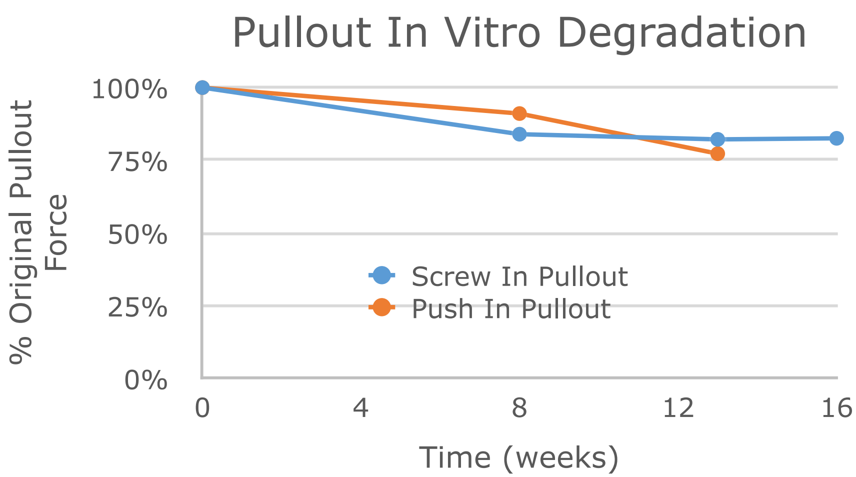


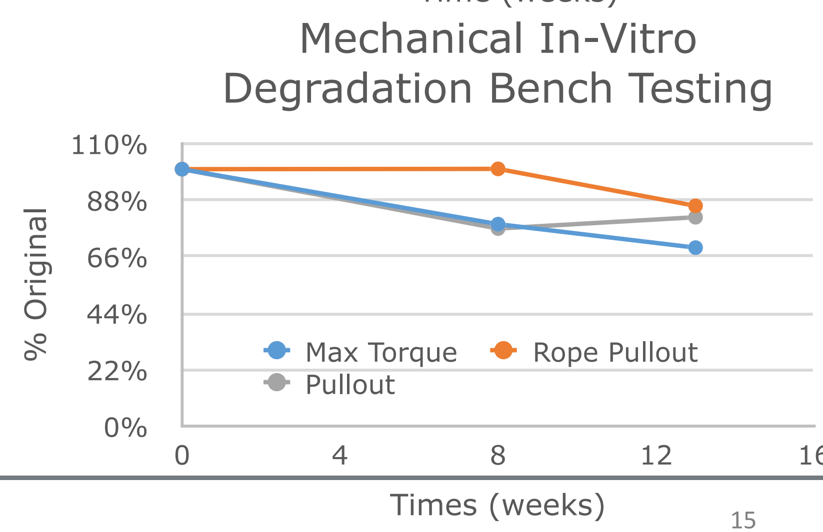


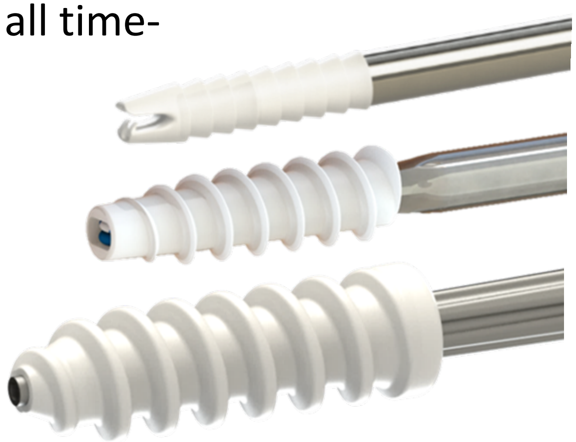
Strength Retention with HA Hybrid Nanocomposite

- With the HA Hybrid composite strength is retained through the healing process

- Both FiberFix™ Anchors & Interference screws demonstrated strength greater than FDA guidance and predicate device benchmark testing in all time-points



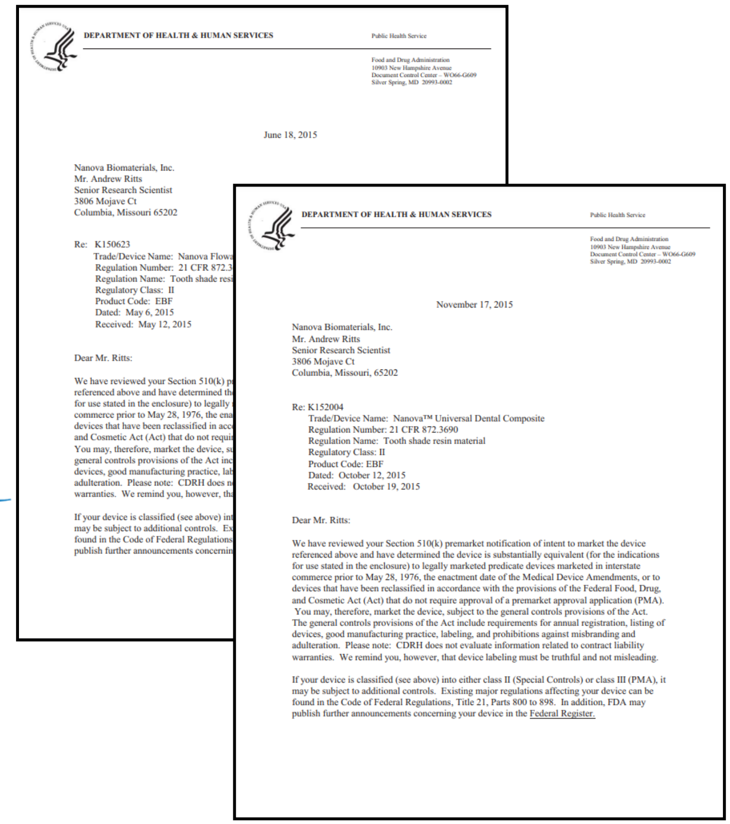




HA Nanofiber Dental Composite: Utilizing HA Nanofiber to improve Mechanical Strength

- Two Class two Implant medical devices
  - ✓ K150623: 6-18-2015
    - ➢ Flowable Composite
  - ✓ K152004: 11-17-2015
    - ➢ Universal Composite

- Contains the same HA nanofiber as the FIberFix™ interference Screw & Suture Anchor



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

June 18, 2015

Nanova Biomaterials, Inc.
Mr. Andrew Ritts
Senior Research Scientist
3806 Mojave Ct
Columbia, Missouri 65202

Re: K150623
Trade/Device Name: Nanova Flowa
Regulation Number: 21 CFR 872.3
Regulation Name: Tooth shade resi
Regulatory Class: II
Product Code: EBF
Dated: May 6, 2015
Received: May 12, 2015

Dear Mr. Ritts:

We have reviewed your Section 510(k) p
referenced above and have determined th
for use stated in the enclosure) to legally
commerce prior to May 28, 1976, the ena
devices that have been reclassified in acc
and Cosmetic Act (Act) that do not requi
You may, therefore, market the device, s
general controls provisions of the Act inc
devices, good manufacturing practice, lab
adulteration. Please note: CDRH does n
warranties. We remind you, however, th

If your device is classified (see above) int
may be subject to additional controls. Ex
found in the Code of Federal Regulations
publish further announcements concernin

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

November 17, 2015

Nanova Biomaterials, Inc.
Mr. Andrew Ritts
Senior Research Scientist
3806 Mojave Ct
Columbia, Missouri, 65202

Re: K152004
Trade/Device Name: Nanova™ Universal Dental Composite
Regulation Number: 21 CFR 872.3690
Regulation Name: Tooth shade resin material
Regulatory Class: II
Product Code: EBF
Dated: October 12, 2015
Received: October 19, 2015

Dear Mr. Ritts:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

NovaPro™ flow

NovaPro™ FILL

Take Home Message

- Superior performance through Patented HA fiber composite technology:
  - ✓ A stronger and tougher composite, bend before they break
  - ✓ Preferred degradation profile
  - ✓ Improved biological properties

- Intellectual properties
  - ✓ Patented: Composition
  - ✓ Patent Pending Push-in anchor design
  - ✓ Trade secret: Materials synthesis and Processing

- Further improved performance from design
  - ✓ Composition may be utilized in other design
- All Manufacturing done at Columbia, MO, USA Facility