Chondrofix® Osteochondral Allograft Clinical Study

Treatment for early intervention of damaged knee cartilage

What exactly is Chondrofix Osteochondral Allograft?

Chondrofix Osteochondral Allograft is made of bone and cartilage tissue that is recovered from a deceased human donor (allograft). This osteochondral (bone & cartilage) allograft is used to repair cartilage damage that is limited to a specific area in the knee.

The graft is cylindrical in shape and comes in a variety of sizes to treat a variety of defect sizes. When used to replace the defect in your knee, this osteochondral graft acts like your natural bone and cartilage tissue, except it has been thoroughly cleaned of blood, fat and other living tissues to improve the chance of healing. The allograft plug is also sterilized and is processed with a step that kills a wide range of viruses.

Why is the Chondrofix Allograft blue?

The graft will have a blue or blue/green color due to the presence of a small amount of left over reagent (substance used for chemical reactions) used during the graft processing to kill viruses. The blue color does not affect the safety or performance of the graft.

How well does Chondrofix Allograft work?

Although there is not yet any data describing how well *Chondrofix* Allograft performs in humans, pre-clinical animal studies showed that *Chondrofix* Allograft provides a smooth, long lasting cartilage surface while integrating well with the surrounding bone (data on file at Zimmer).

Is Chondrofix Allograft safe?

Yes, but there are risks associated with any surgical procedure.

Medical and surgical conditions or complications that apply to any surgical procedure may occur during or following implantation of the *Chondrofix* Allograft. The graft may contain trace amounts of processing reagents, which could cause a reaction if you are sensitive or allergic to any of these chemicals.

Your surgeon is responsible for evaluating you and informing you of the risks associated with the surgery, including any possible complications or adverse events.

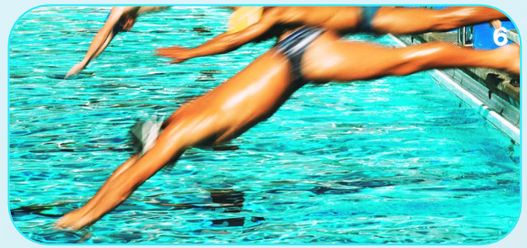
Chondrofix Allograft is human tissue that has been minimally processed to preserve important characteristics of the original donor tissue. It has also been processed to get rid of or inactivate bacteria and viruses that may be found in human tissue grafts.

Donor screening, processing treatments and laboratory testing follow stringent specifications to reduce the risk of infectious agent transmission; however, all human tissue has the potential to transmit infectious diseases, including your *Chondrofix* Allograft. This risk is extremely low due, in part, to the evaluation of potential donors of human tissue to determine eligibility (ask your surgeon for further details). In addition, *Chondrofix* Allograft is processed to remove blood, cells and fat from the tissue and is sterilized to kill bacteria and other microorganisms.

Although rates of infection risk are not known for *Chondrofix* Allografts specifically, there are data available regarding allograft tissue (bone, tendon, or cartilage). Over the past 20 years, there have been only 12 reported cases of viruses (HIV, Hepatitis) from allografts out of more than 10 million allografts transplanted in the US[1]. The four reported cases of HIV transmission from allograft to patient occurred in the 1980s, before testing for HIV was done. Data from 2005 estimated an incidence of infection from allografts at 0.0004% per year[2].

Is Chondrofix Allograft approved by the FDA?

Since *Chondrofix* Allograft is minimally processed donated human tissue meant for human transplant use, it does not require pre-approval from the Food and Drug Administration (FDA). Although the graft does not get approved by the FDA, the tissue and final graft is handled only by organizations appropriately registered with the FDA, and it is processed, tested, packaged, and distributed in compliance with stringent regulations. *Chondrofix* Allograft is processed and packaged by LifeNet Health, a FDA registered tissue bank who is accredited with the American Association of Tissue Banks (AATB). Also, *Chondrofix* Allograft is "listed" with the FDA, meaning that the FDA has been notified that the graft is being used.



Can I receive Chondrofix Allograft without being in the clinical study?

Yes. *Chondrofix* Allograft is an available medical product that does not require you to be in the study to receive it. Keep in mind, if you choose to enroll in the clinical study, you may be able to help other people in the future who have similar problems with their knee(s).

What is the difference between Chondrofix Allograft and other treatments?

There are several possible treatments available for repairing the damaged cartilage in your knee. These treatments can include repair by autograft or allograft tissue.

Let's take these one at a time.

- Autograft refers to tissue taken from you. In other words, your surgeon will remove bone-cartilage tissue from somewhere else in your knee (e.g. the outside edge of your knee cartilage) and use it to repair your damaged cartilage. There are both benefits and risks to this treatment option (please ask your surgeon for details); however, this procedure may cause pain in the area where the tissue was taken[3].

- Allograft refers to tissue that is taken from a deceased human donor. The tissue can be fresh meaning it is unprocessed and refrigerated for a short period of time before being implanted into a patient. The tissue can also be frozen meaning it is unprocessed but stored in a freezer for longer storage then thawed before implantation. Both fresh and frozen allografts are used for repair of a patient's cartilage in much the same way as *Chondrofix* Allografts. However, one limitation of traditional allografts is low supply of these tissues for various reasons which can cause delays in scheduling surgical treatment.

- *Chondrofix* Allograft is an allograft tissue as well but does not have the same supply limitations because it can be stored at room temperature for long periods of time. This means you have more flexibility in deciding when you want to have surgery. The other benefit of *Chondrofix* Allografts is a further decrease in the risk of getting a disease or infection from the allograft tissue because of additional processing steps that protect against transmission of disease due to bacteria and viruses.

Who qualifies for the clinical study?

The following is not a complete list of inclusion/ exclusion criteria. The clinical study site will evaluate you as a potential study patient based on a complete list.

Inclusion Criteria

- Male and non-pregnant female subjects between 18 and 70 years.
- If female: must be actively practicing a contraception method & not have plans to get pregnant in the next 2 years
- MRI or arthroscopic evaluation that exhibits up to 2 ICRS Grade 3 or 4 cartilage lesion(s) or an OCD located on the femoral condyle or trochlear groove of the knee. Lesion < 8 cm^2 and < 10 mm of bone involvement
- Localized knee pain unresponsive to conservative treatment (e.g., medication, bracing, physical therapy) and/or surgical intervention
- Opposite knee has no symptoms, is stable and fully functional.

Exclusion Criteria:

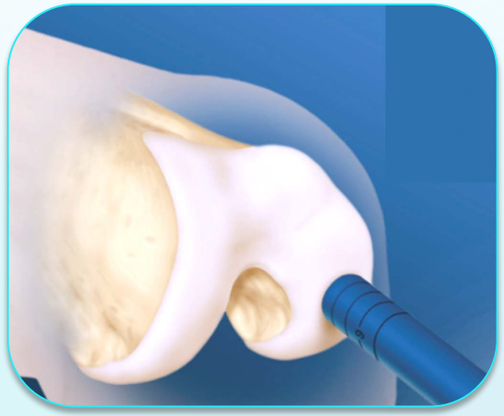
- Participation in another clinical trial or prior participation within three months of surgery,
- Cartilage lesion is not adequately shouldered or has bipolar cartilage involvement with > ICRS Grade 2 lesion,
- Taking pain medication (other than NSAIDs or acetaminophen), anticoagulants, or corticosteroids for conditions unrelated to the knee condition
- Prior knee surgery within last six months
- Other procedures (e.g., additional cartilage repair, distal realignment, ligament reconstruction, etc.) required during surgery
- Total meniscectomy of the index knee,
- Uncorrected mal-alignment of the knee >5 ,
- Prior HA or cortisone injection in knee within three months of surgery.
- Contraindications for MRI,
- HIV
- Workman's compensation and/or litigation related to the knee

What would the clinical study involve?

The clinical study will be performed at up to six different centers throughout the U.S. and will enroll approximately 50 patients.

If you choose to sign the Informed Consent Form for the study, undergo implantation of the *Chondrofix* Allograft, and meet certain criteria during surgery, you will be asked to return for follow-up visits for up to **five years** and will undergo additional X-rays and MRIs during this follow-up period.

During the follow-up visits you will have an examination and complete some questionnaires that ask about your health, how well your knee is working and feeling, what medications or therapies you are taking and other related questions.



Why choose Chondrofix Allograft as your treatment?

Since *Chondrofix* Allograft is created from donated human tissue, the procedure requires only one surgery and does not "borrow" bone from anywhere else in your body. The use of *Chondrofix* Allograft over other fresh or frozen allograft tissues may also lower the chance for bacterial or viral infection from donor tissue.

For patients who suffer knee pain and/or functional limitations, this study will investigate how well the *Chondrofix* Allograft performs in your body to repair your cartilage defect.

Contact Information/ Research Team

References:

1. AAOS 2008 Biological Implants Committee Scientific Exhitit, http://www.aaos.org/research/committee/biologic/logic.asp
2. CDC, FDA & HHS 2005 Workshop on Preventing Organ & Tissue Allograft-Transmitted Infection: http://www.cdc.gov/ncidod/dhqp/pdf/bbp/organ_tissueWorkshop_June2005.pdf
3. Gautier E, et al. (2002) JBJS-Br 84:237–244