





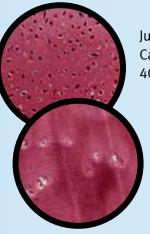


DeNovo NT Graft – Advancing the Science of Cartilage Repair.

DeNovo NT Natural Tissue Graft is a juvenile cartilaginous allograft tissue intended to provide surgeons with an early-intervention option for the repair of articular cartilage in a wide range of anatomic focal cartilage defects. It offers a single-stage procedure with fibrin fixation that eliminates the need for harvesting a periosteal flap. With DeNovo NT Graft, Zimmer demonstrates its commitment to leadership in providing surgeons – and their patients – with a complete continuum of joint care.

Juvenile Cartilage Tissue

DeNovo NT Graft consists of scaffold-free living articular cartilage, displaying biochemical properties similar to those of articular cartilage found in young, healthy joints.



Juvenile Cartilage 400X

> Adult Cartilage 400X



Cartilage Injury and Treatment

- Adult articular cartilage has limited capacity for self-repair.¹
- Untreated focal defects begin a cycle of cartilage breakdown, arthritic degeneration and ultimately, the need for joint replacement.

DeNovo NT Graft offers a simple alternative to focal cartilage defect treatment.

Pre-Clinical Evidence from Studies of Bovine Chondrocytes*

Juvenile bovine cartilage has a significantly higher cell density than adult cartilage (p<0.05), and juvenile bovine chondrocytes have significantly higher proliferation rate than adult chondrocytes (Day 3, p<0.01).

Relative Light Units/Second (x10⁴)

60

40

20

Juvenile

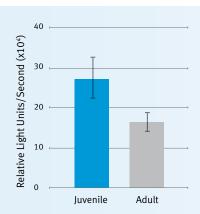
Day 1

Day 3

Adult

Clinical Experience

- Human clinical experience includes
 6 years of implant history and greater
 than 7,000 grafts.
- DeNovo NT Graft has been used to treat focal defects in a wide range of anatomical applications, including:
 - Knee (i.e., condyle, trochlea, patella, tibial plateau)
 - · Foot and ankle (i.e., talus, MPJ)
 - · Elbow
 - Shoulder (i.e., humeral head, glenoid)
 - · Hip (i.e., acetabulum, femoral head)
- Clinical trials in both the ankle and knee demonstrate significant improvement in patient reports of pain, function, and activity scores (KOOS, AOFAS, FAAM, and VAS Pain Scale)²⁻⁴

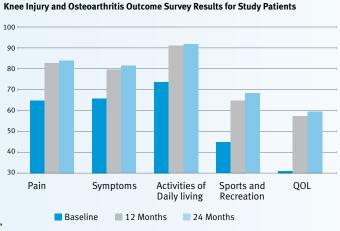


Juvenile

Adult

Cells/g of Cartilage (x10^o)

Juvenile chondrocytes synthesize significantly greater amount of GAG than adult chondrocytes (p<0.05). ("GAG" is glycosaminoglycan, a naturally occurring carbohydrate found in cartilage that decreases inflammation and serves as the building blocks of new cartilage.)



Outcome scores in 25 knee patients 24 months following *DeNovo* NT Graft implant. Significant improvement over baseline is seen for pain, symptoms, functions and sports (p<0.05).





MRI of 35 year old male with medial talus lesion, preoperative (top) and 6 months after *DeNovo* NT Graft surgery (bottom).

^{*} Animal Study results are not necessarily predictive of human results.

Comparing Cartilage Defect Repair Treatment Alternatives

	Defect Characteristics	Tissue Characteristics	Procedure Characteristics
<i>DeNovo</i> NT Graft	Chondral defects up to 5 cm² (greater at surgeon's discretion)	Juvenile (≤ 13 yrs) hyaline cartilage, risk of disease transmission	Single stage surgery, simple technique with fibrin fixation, may be done arthroscopically, used in multiple joints including knee (patellofemoral & condyle)
Autologous Chondrocyte Implantation (ACI)	Chondral femoral defects; routinely 5 to 10 cm ²	Adult autologous chondrocytes	One or two-stage surgical procedure, fixation from scaffold or cover subsequent reoperations common ⁵
Bone Marrow Stimulation*	Chondral; limited treatment area < 2 cm ²	No tissue implanted, fibrous repair tissue ⁶⁻⁷	Single stage surgery, simple technique, may be done arthroscopically
Osteochondral Autograft	Osteochondral; limited treatment area < 2 cm ²	Adult autologous tissue from non-weight bearing surface	Single stage complex procedure, perpendicular access to defect required, donor site morbidity
Osteochondral Allograft	Osteochondral; large defects > 2 cm ²	Adult allograft tissue, risk of disease transmission, typical wait period for graft availability	Single stage complex procedure, perpendicular access to defect required
Micronized Cartilage Matrix (BioCartilage®)	Chondral; limited treatment area < 2 cm ²	Dehydrated, micronized adult cartilage	Single stage surgery, augment to bone marrow stimulation procedures, no published clinical evidence

^{*} e.g., debridement, microfracture, chondroplasty, subchondral drilling, etc.

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- 5. Harris, Siston, Brophy, Lattermann, Carey, and Flanigan. Failures, re-operations and complications after autologous chondrocyte 400 implantation a systematic review. *Osteoarthritis and Cartilage*, 2011. 19: 779-791.
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