

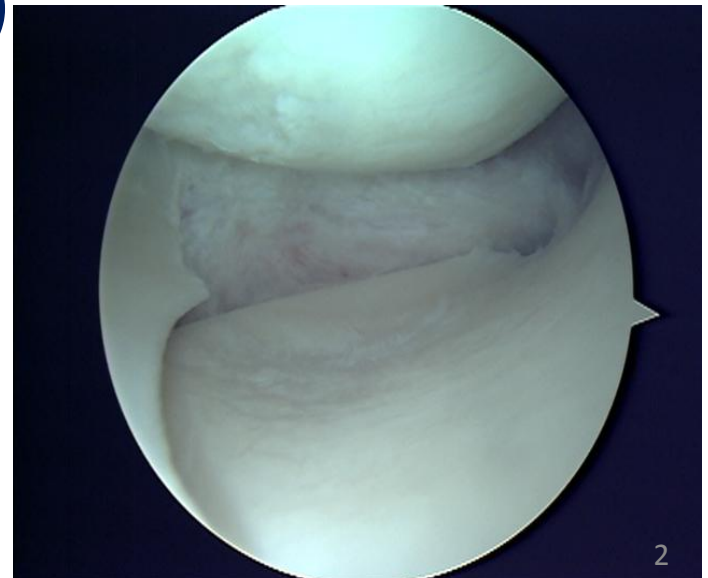
# **ACTI***fit*<sup>®</sup> Meniscal Scaffold

**New Treatment Option  
for  
Irreparable Partial Meniscal Tears**

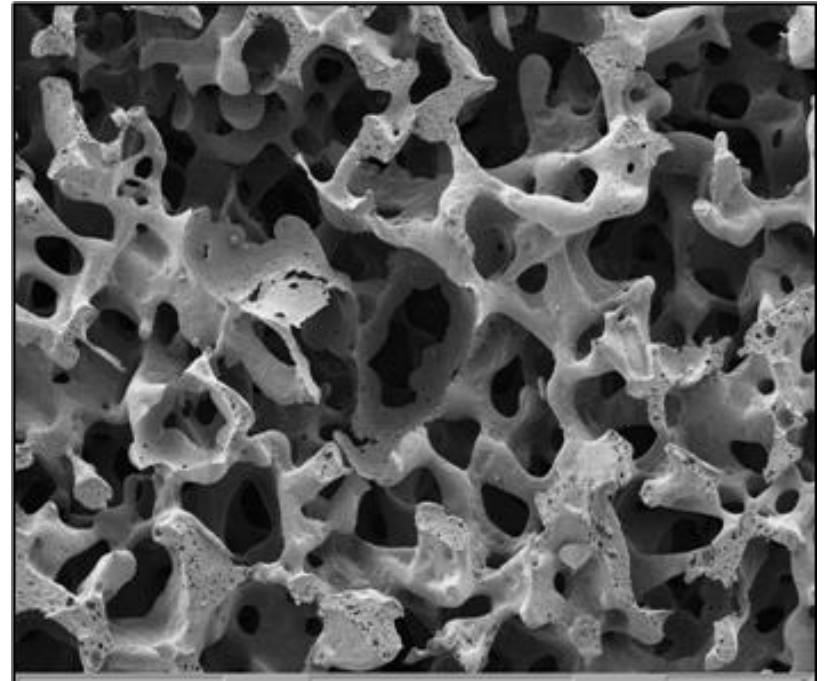


# Partial Meniscectomy

- Each year > 1.5 million partial Meniscectomies in EU and the US (Verdonk 2008)
- Only treats symptoms
- Removal of weight-bearing meniscal tissue results in gradual degeneration of cartilage (Fairbank, 1948; Rodkey 1999)



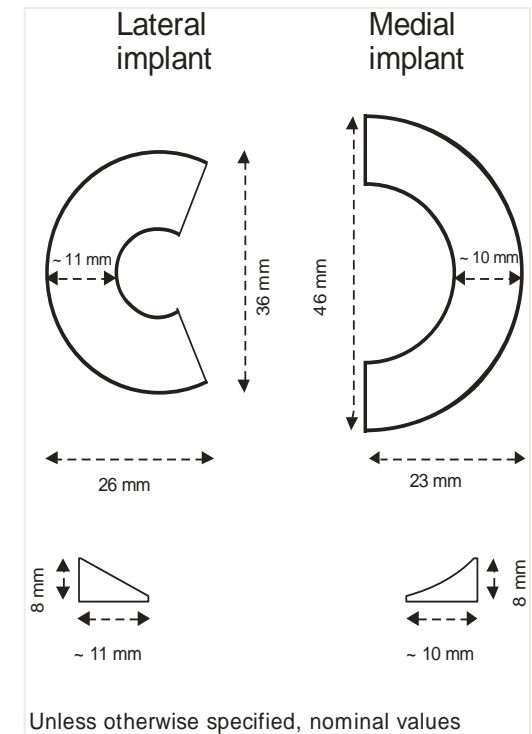




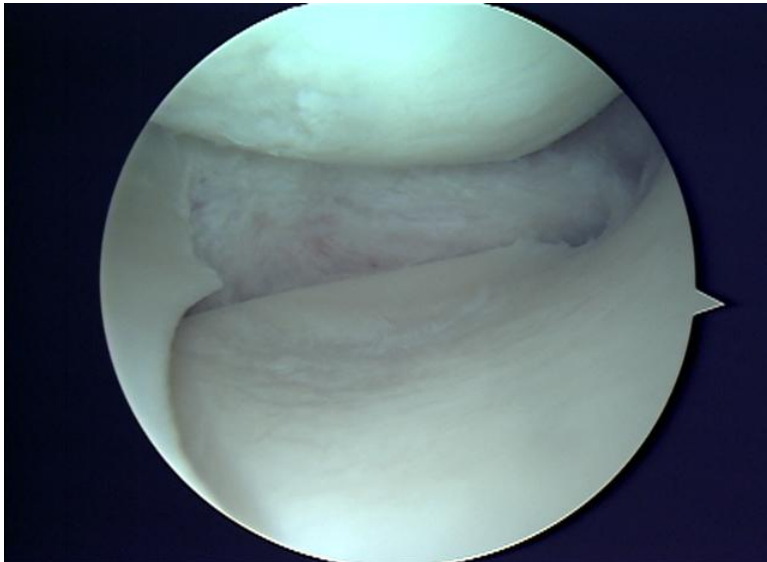
Highly porous scaffold made from a biocompatible, slowly degrading  
**aliphatic polyurethane**

# Device Description

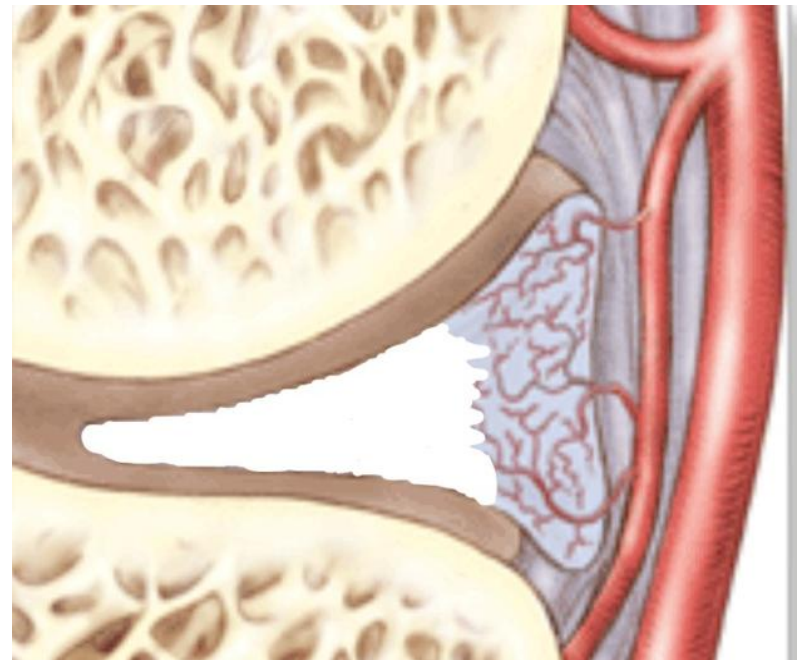
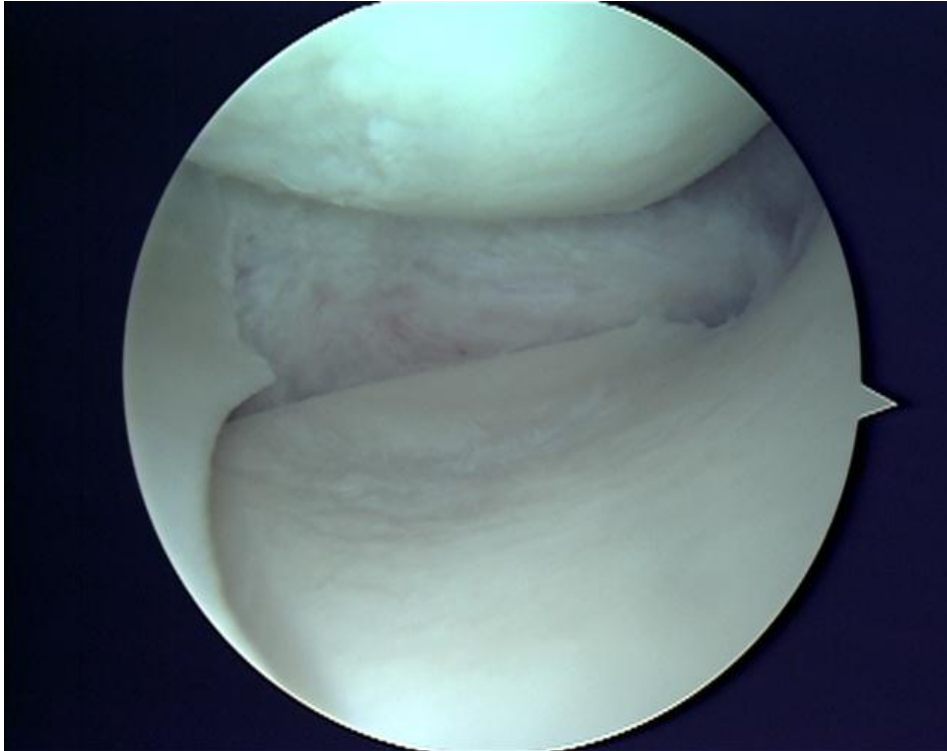
- Single-component, biodegradable meniscal scaffold
- Dimensions based on human meniscus
- Available in medial and lateral configurations
- Implanted via standard arthroscopic procedure



A biodegradable, porous scaffold, designed to support the formation of new tissue, using the bodies own physiological pathways for healing.



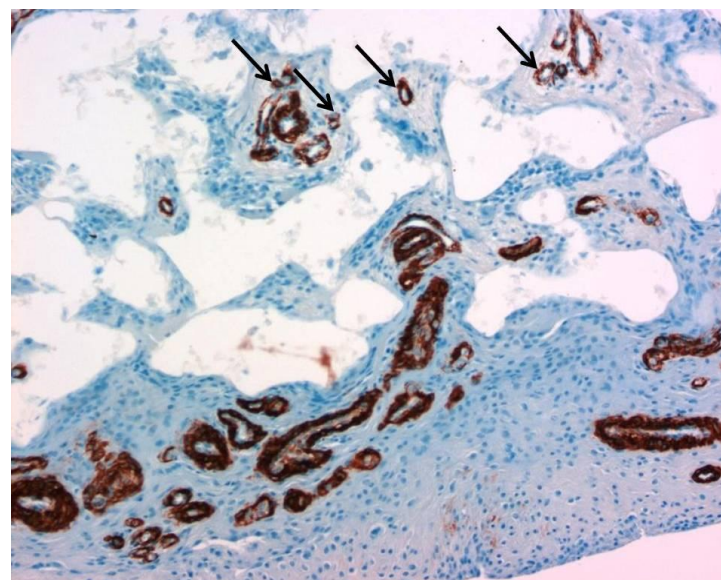
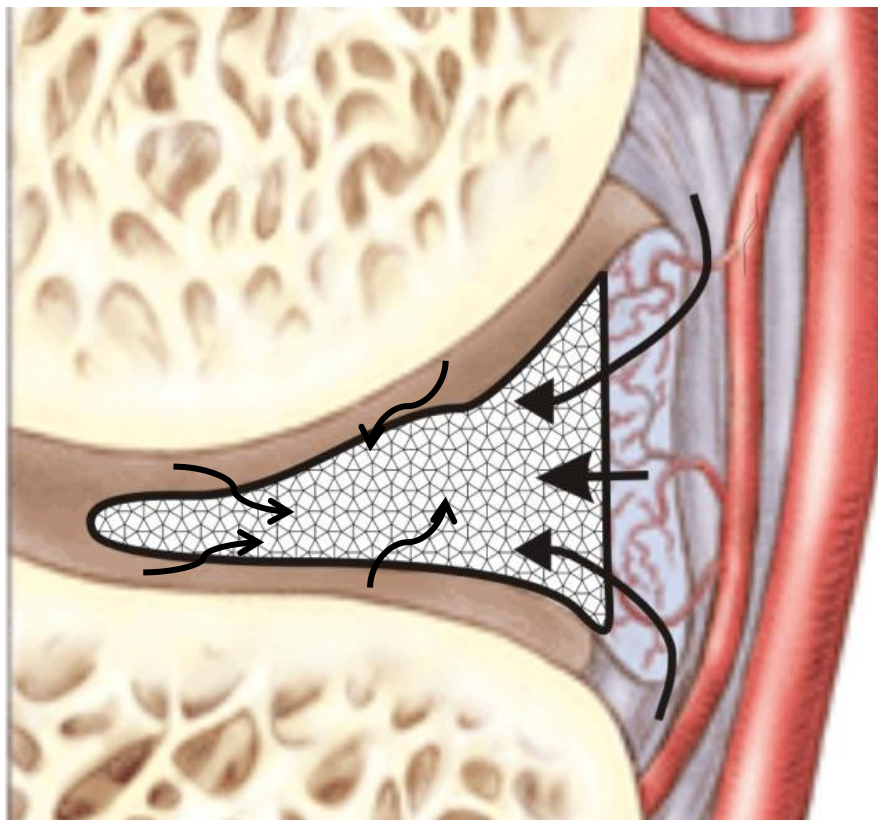
# Principles of Operation



Partial meniscectomy



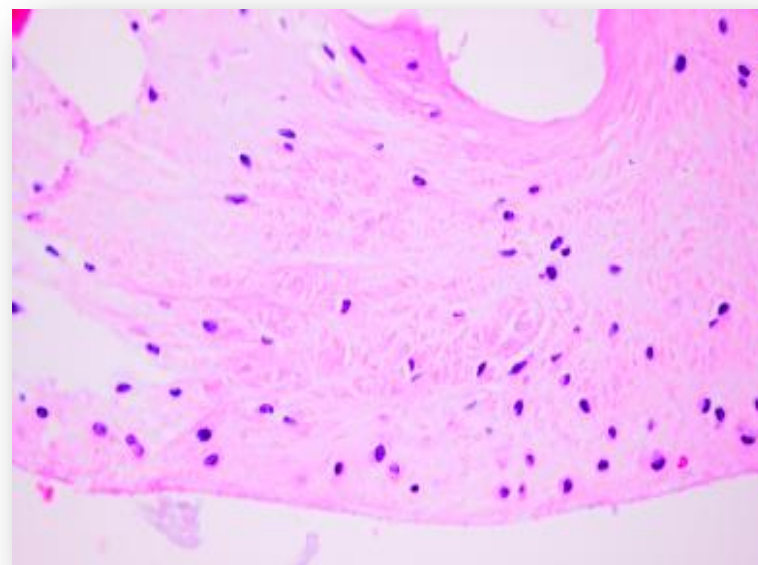
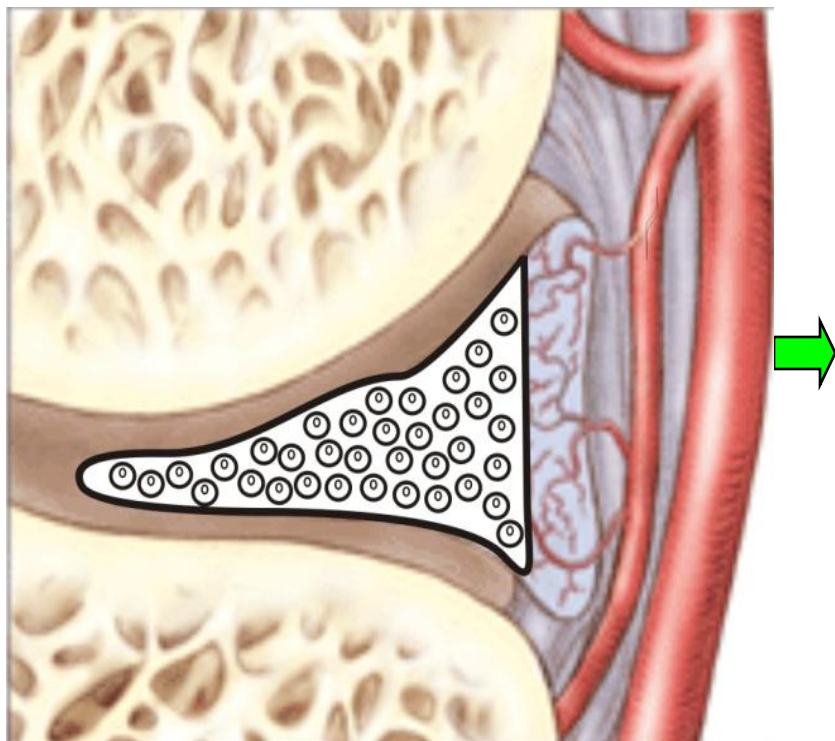
# Principles of Operation



Actifit® attached to the vascularized zone of the meniscus, allows tissue regeneration through cellular infiltration and vascular ingrowth.



# Principles of Operation

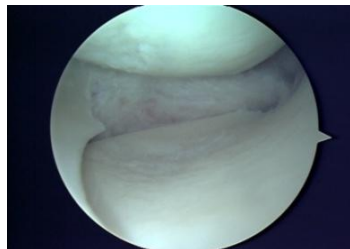


Regenerated functional tissue with meniscus-like characteristics

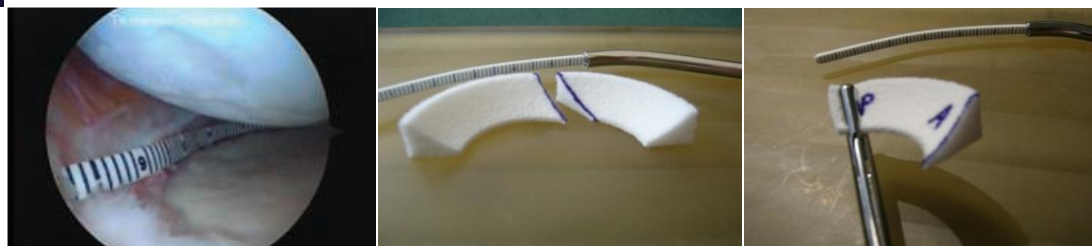
Photo courtesy of Dr R Forsyth, UGhent, Belgium

# Implantation Procedure

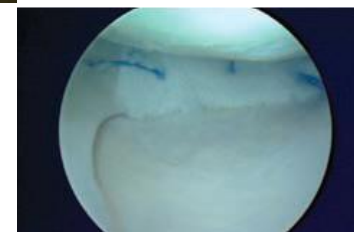
## 1. Debride the damage



## 2. Measure, Oversize by 10%, Cut and Insert



## 3. Suture in Place



Ease of implantation due to optimized properties;  
Suture pull-out and tear strength, flexibility.

# Criteria for Optimal Outcomes using ACTI*fit*<sup>®</sup>

- 18-50 years old – skeletally mature patient
- Partial lesion with stable rim (NB intact popliteal bridge in the lateral indication)
- Both horns present
- Stable, well aligned knee
- ICRS classification <3
- Patient understands the importance of, and commits to adhere to rehabilitation program



## **Safety and Efficacy Study**

# Study Design

- Prospective, single-arm, multi-centre, clinical investigation designed to assess the safety and efficacy of Actifit<sup>®</sup> indicated for partial meniscus substitution
- VAS, performed at baseline ,1 week, 3, 6, 12 and 24 months post-implantation
- IKDC, KOOS and Lysholm efficacy scores performed at baseline , 3, 6, 12 and 24 months post-implantation
- MRI Follow-up at 1 week, 3, 12 and 24 months post-implantation
- Relook and Biopsy at 12 months

# Investigators

## *NAME*

## *AFFILIATION*

- **Prof R Verdonk** - University Hospital Gent
- Prof P Beaufils - Centre Hospitalier de Versailles
- Prof P Neyret - Centre Livet de Lyon
- Prof H Paessler - Atos Praxisklinik Heidelberg
- Dr R Cugat - Hospital Quirón de Barcelona
- Dr P Colombet - Clinique de Merignac Bordeaux
- Dr H Laprell - Lubinus Clinicum of Kiel
- Dr P Djian - Institut Nollet Paris
- Prof J Bellemans - University Hospital Pellenberg



# Baseline Characteristics

<b>TOTAL of 52 patients</b>	<b>Medial</b>	<b>Lateral</b>
	<b>N = 34</b>	<b>N = 18</b>

---

Age (years)

Mean  $\pm$  SD: **30.8  $\pm$  9.4**

Sex (n)

Male: **39 (75%)**

Female: **13 (25%)**

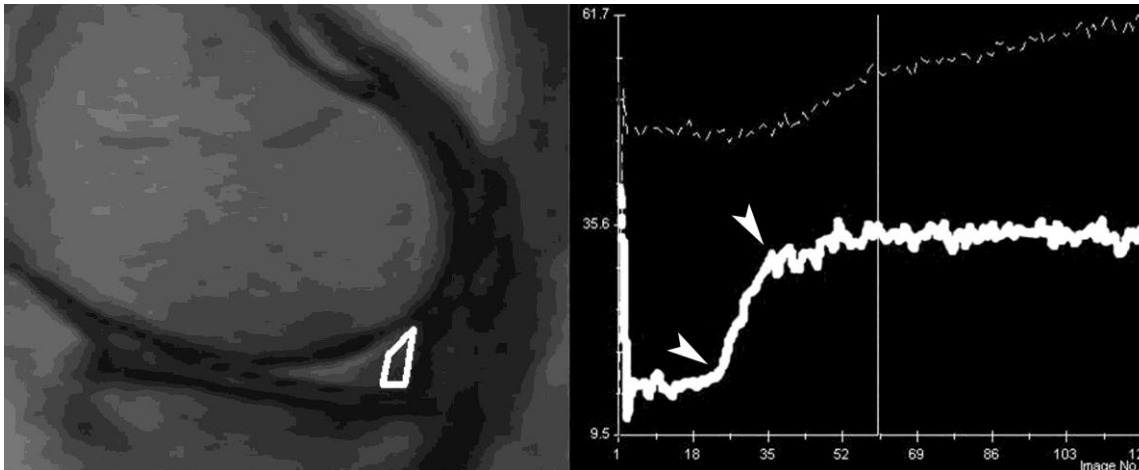
Longitudinal length (mm)

Mean  $\pm$  SD: **47.1  $\pm$  10**

**88.4% had one or more previous surgeries**

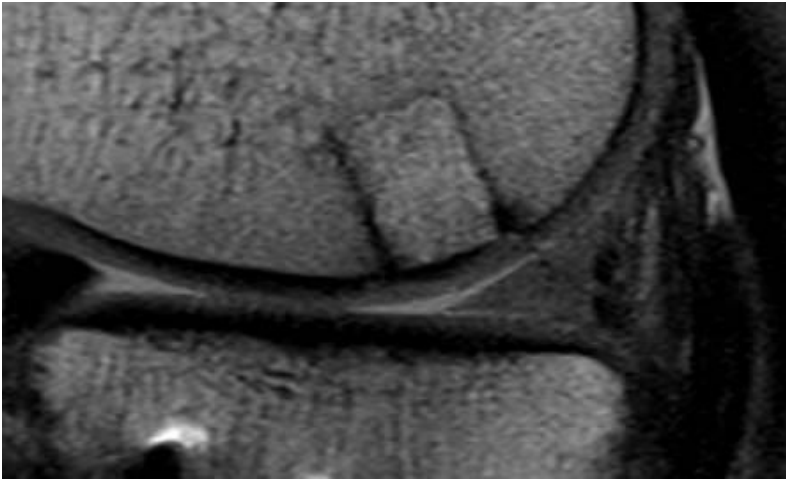
## Imaging Results: DCE-MRI

- Dynamic Contrast Enhanced MRI depicts vascular tissue ingrowth in a non-invasive manner (Tokuda *et al* 2005, Verstraete *et al* 1994)
- The outer half of the scaffold was set as region of interest
- At 3 months evidence of tissue ingrowth into the scaffold in 81.4%

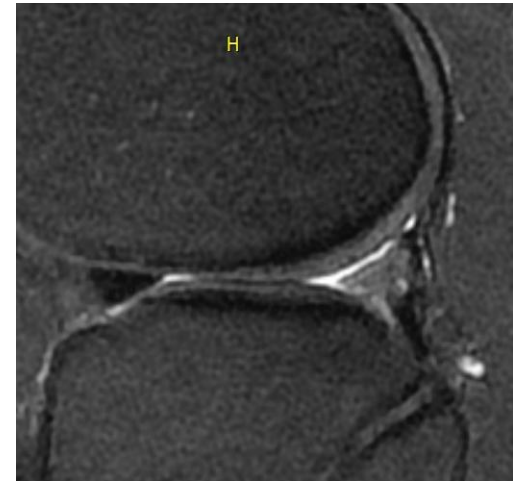


Increase of signal intensity in the first pass phase (between arrowheads) can only be explained by the presence of blood vessels in the device.

# Imaging Results: Meniscus



**Complete refill of medial meniscus defect in patient with an osteochondral plug in an area overlying the polyurethane scaffold**

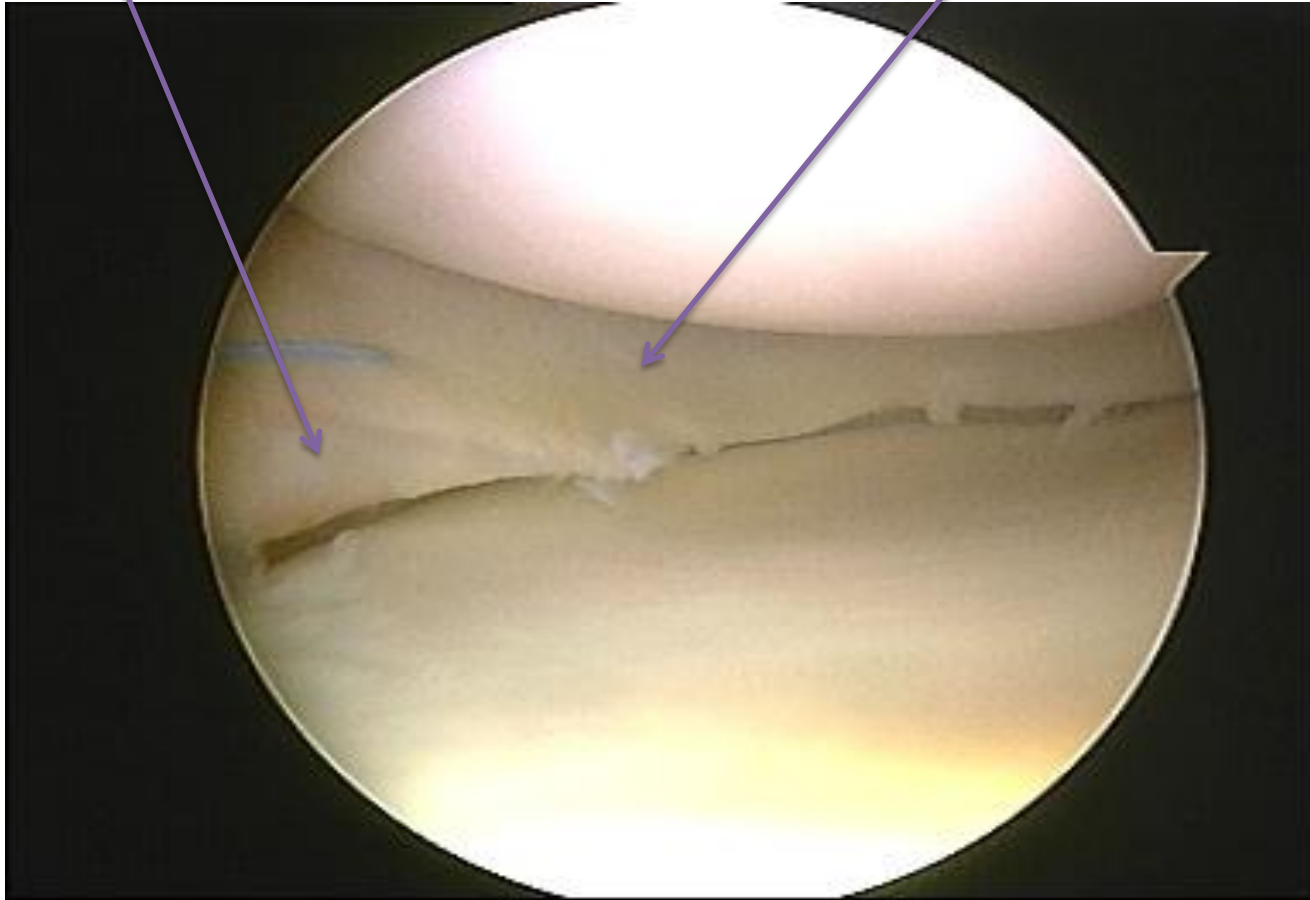


**Complete refill of lateral meniscus defect at 24 months**

# RELOOK Arthroscopy at 12 Months

Native Meniscus

Actifit



09-003

Photo courtesy of Professor Bellemans , Leuven, Belgium

## MRI Results at 24 months \*

- At week 1, all scaffolds were well-positioned illustrating reproducible surgical technique
- As expected signal intensity is different from normal meniscus tissue
- Scaffold is clearly visible at week 1, 3, 12 and 24 months, allowing non-invasive assessment of the tissue populated scaffold



\*n=40 at 24 months

*Courtesy of Dr W Huysse, UZ Gent.*

## MRI Results at 24 months \*

**No evidence of cartilage damage related to the device.**

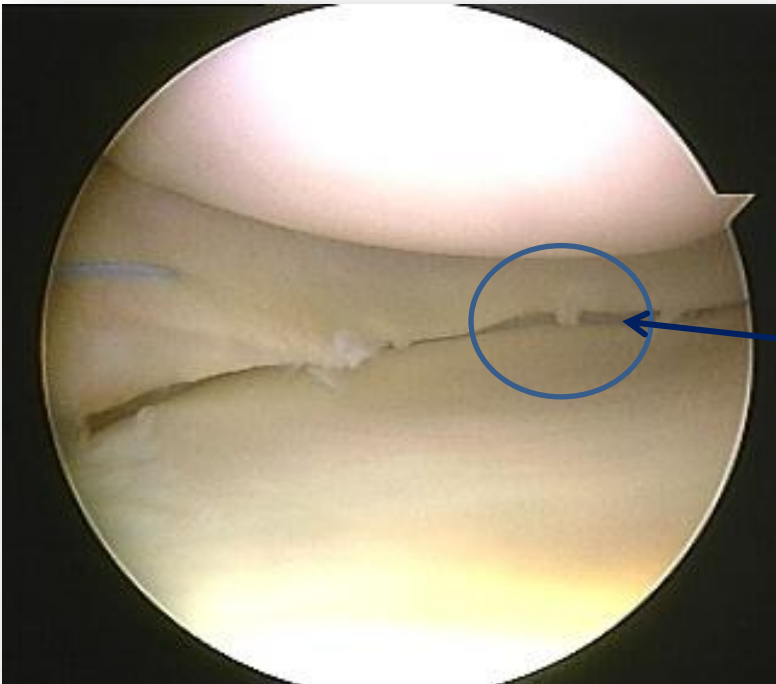


**Example of improved cartilage at 24 months**

\*n=40 at 24 months

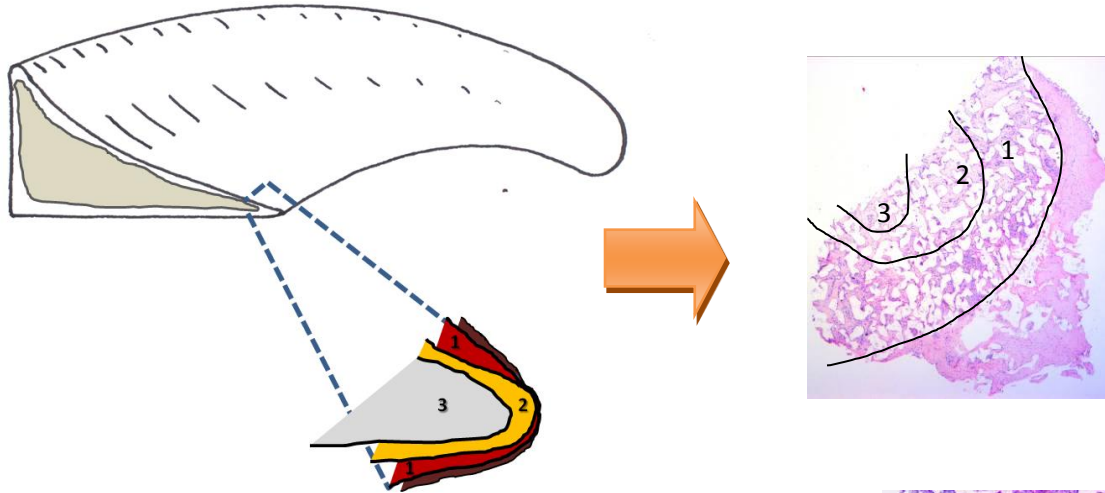


# Histology Results of 1 year Biopsies

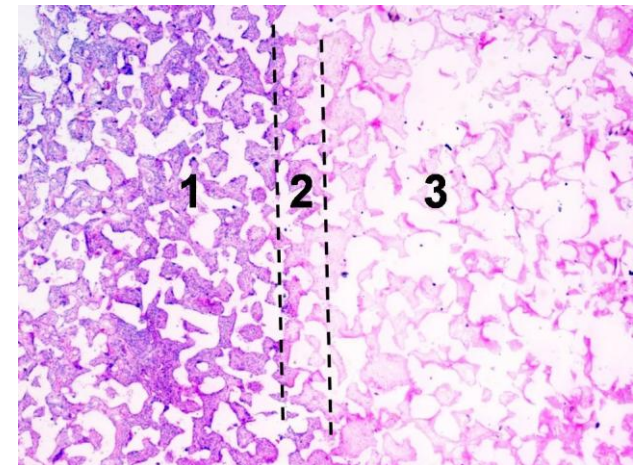


All biopsies are taken from  
inner free edge of  
regenerated tissue

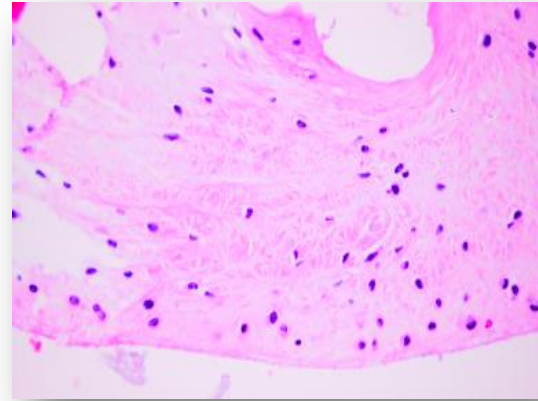
# Histology Results ( n=44 )



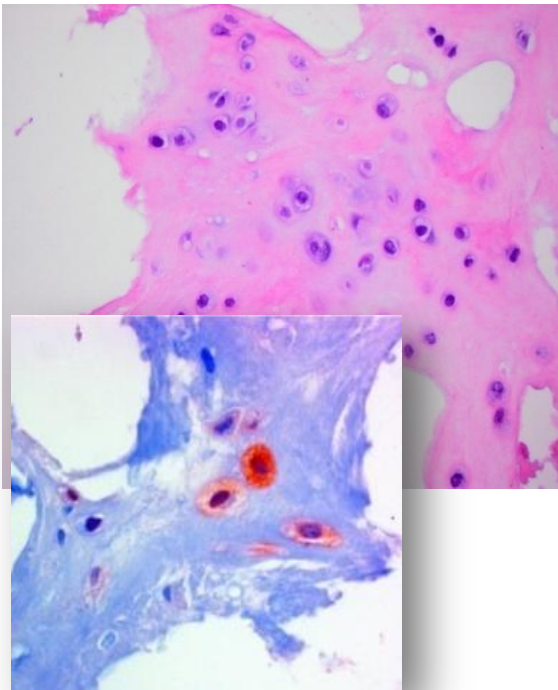
- Fibrous capsule
- Layer 1: vascular, hypercellular
- Layer 2: avascular, hypercellular
- Layer 3: avascular, hypocellular



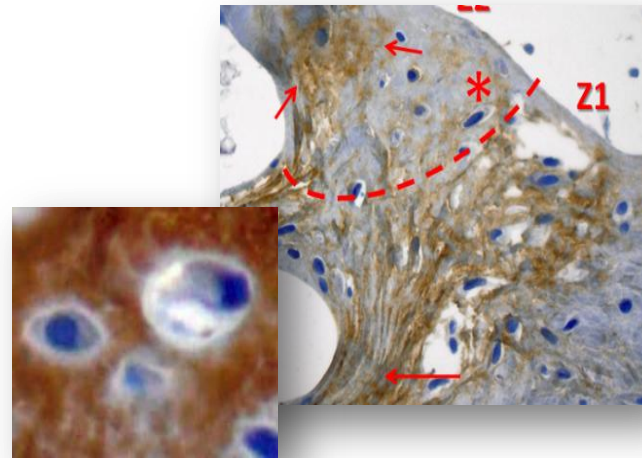
# Meniscus-like Tissue at 1 Year



Biopsy from inner free edge of regenerated tissue at 12 M



S-100 positive chondroblast-like cells



Positive staining for collagen type 1

# Histology Results Summary

- **Predictable cellular organization**
- **Repopulation** of all biopsies with vital cells
- No case of tissue necrosis or cell death - illustrating the biocompatibility of the **ACTIfit®** scaffold
- **New tissue consistent** with ongoing process of regeneration, maturation and remodeling towards tissue with meniscus like tissue characteristics.
- Scaffold material is still present in all biopsies at one year

# Safety Summary

- No inflammatory reaction to the device or its degradation products observed **during relooks**
- No inflammatory reaction to the device or its degradation products observed **in biopsies**
- **No device related SAEs**
- **No sign of cartilage damage** related to the device

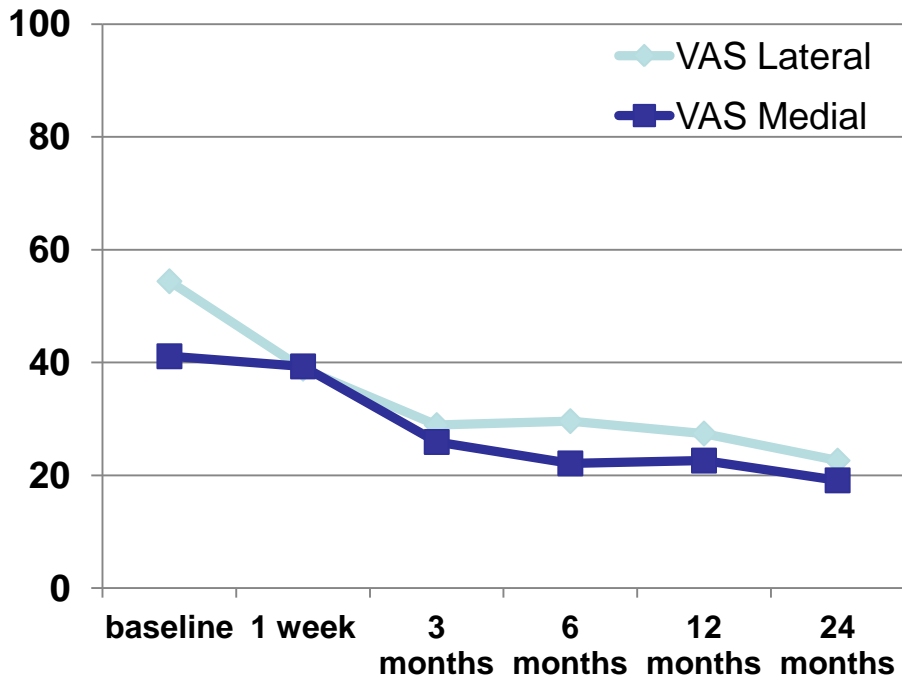


**Clinical Efficacy**



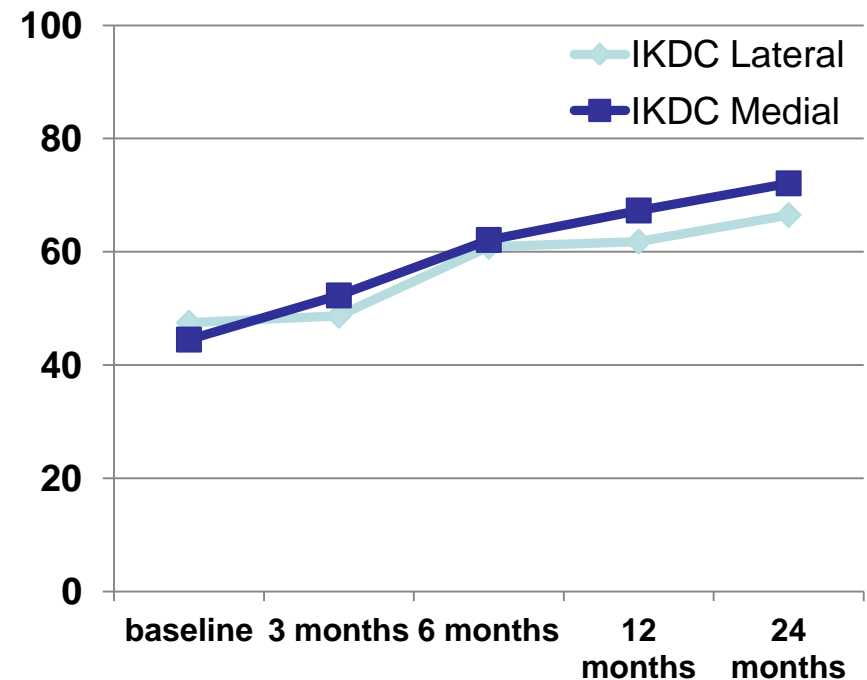
# Statistically and Clinically<sup>‡</sup> Significant Pain Reduction and Functional Improvement: Continued improvement over 36 months!!!

## VAS\*



Lower Scores=Less Pain

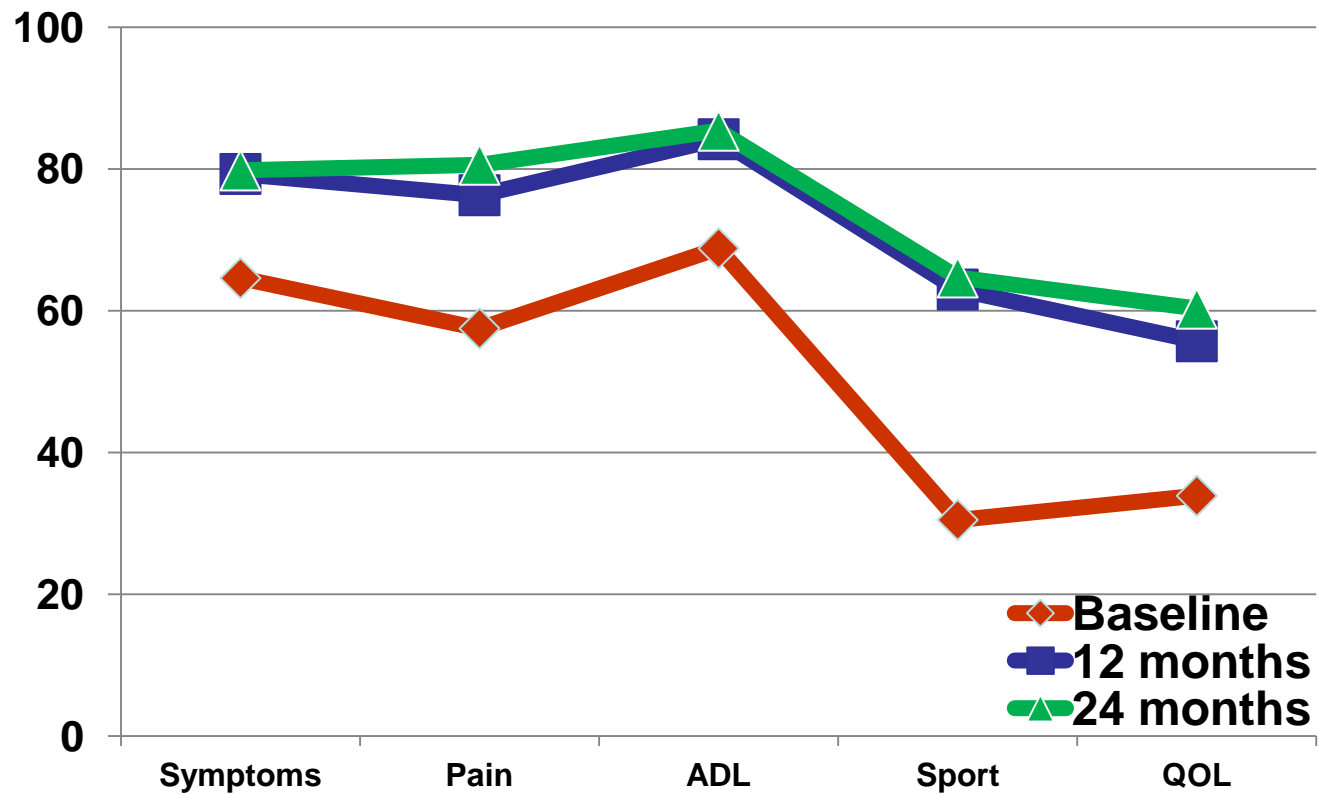
## IKDC\*



Higher Scores= Better Performance

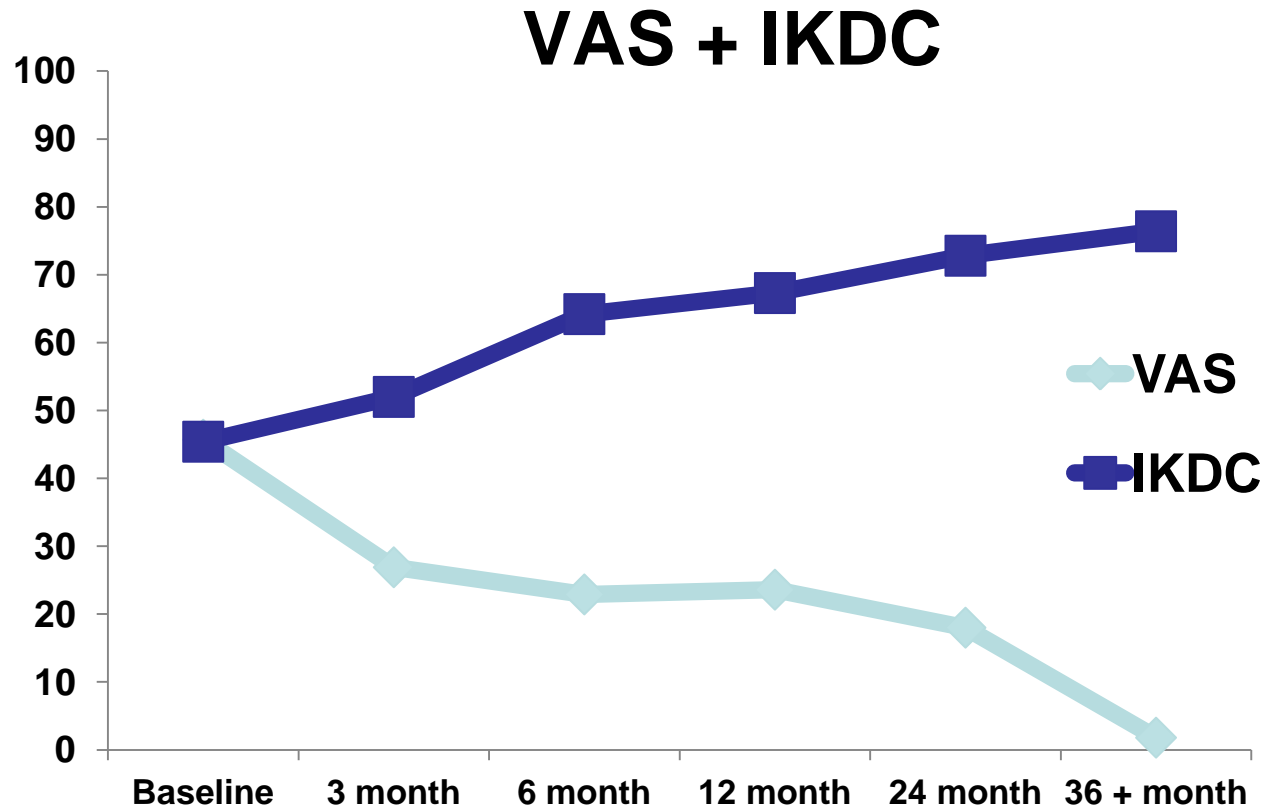
<sup>‡</sup> Kelly AM. Emerg Med J. 2001  
Irrgang JJ. Am J Sports Med. 2006

## KOOS: Continued Improvement over 36 Months!!!



**Higher Scores=Better Functionality**

# Demonstrated Long Term Success for the Patient!



# Early 48 month MRI

- 10 subjects so far with 48 month MRI
- ICRS scores between baseline and 48 months
  - 6 stable
  - 1 worse
  - 3 improved

## Tissue Ingrowth After Implantation of a Novel, Biodegradable Polyurethane Scaffold for Treatment of Partial Meniscal Lesions

René Verdonk,<sup>\*†</sup> MD, PhD, Peter Verdonk,<sup>†</sup> MD, PhD, Wouter Huysse,<sup>‡</sup> MD,  
Ramses Forsyth,<sup>§</sup> MD, PhD, and Eva-Lisa Heinrichs,<sup>||</sup> MD

*Investigation performed at Ghent University Hospital, Ghent, Belgium*

---

**Background:** A novel, biodegradable, aliphatic polyurethane scaffold was designed to fulfill an unmet clinical need in the treatment of patients with irreparable partial meniscal lesions.

**Hypothesis:** Treatment of irreparable partial meniscal lesions with an acellular polyurethane scaffold supports new tissue ingrowth.

**Study Design:** Case series; Level of evidence, 4.

**Methods:** Fifty-two patients (with 34 medial and 18 lateral lesions) were recruited into a prospective, single-arm, multicenter, proof-of-principle study and treated with the polyurethane scaffold. The scaffold was implanted after partial meniscectomy using standard surgeon-preferred techniques for suturing. Tissue ingrowth was assessed at 3 months by dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) and at 12 months by gross examination during second-look arthroscopy, in the course of which a biopsy sample from the inner free edge of the scaffold meniscus was taken for qualitative histologic analysis.

**Results:** Tissue ingrowth at 3 months was demonstrated on DCE-MRI in 35 of 43 (81.4%) patients. All but one 12-month second-look (43 of 44 [97.7%]) showed integration of the scaffold with the native meniscus and all biopsy specimens (44) showed fully vital material, with no signs of cell death or necrosis. Three distinct layers were observed based on morphologic structure, vessel structure presence or absence, and extracellular matrix composition.

**Conclusion:** The DCE-MRI demonstrated successful early tissue ingrowth into the scaffold. The biopsy findings demonstrated the biocompatibility of the scaffold and ingrowth of tissue with particular histologic characteristics suggestive of meniscus-like tissue. In conclusion, these data show for the first time consistent regeneration of tissue when using an acellular polyurethane scaffold to treat irreparable partial meniscus tissue lesions.

**Keywords:** Actifit; meniscus; biodegradable scaffold; meniscectomy; polyurethane scaffold; partial meniscectomy

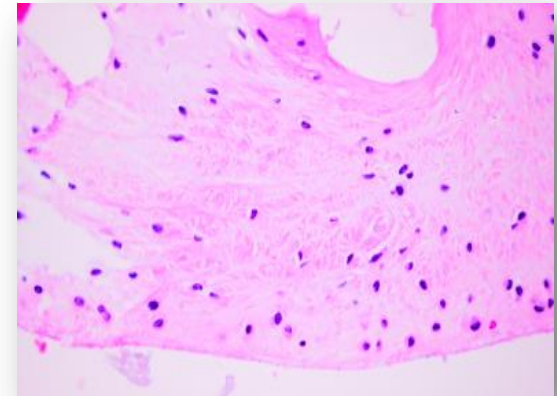
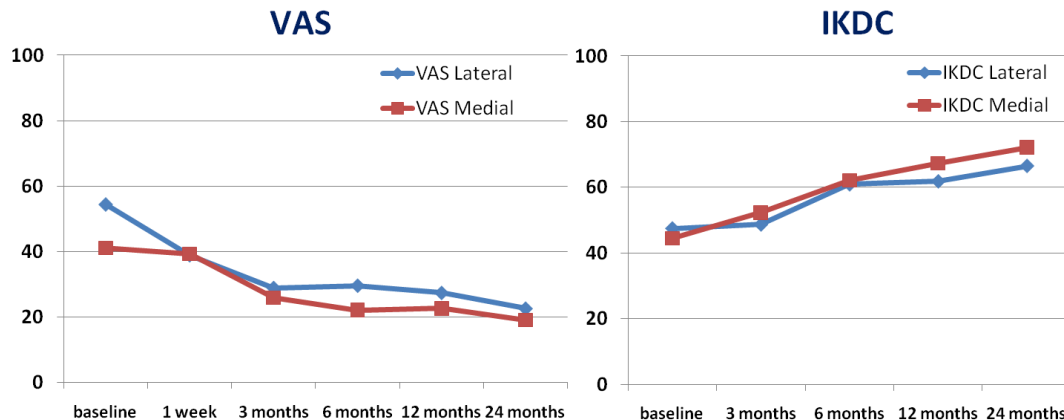
---

## Successful Treatment of Painful Irreparable Partial Meniscal Defects With a Polyurethane Scaffold

### Two-Year Safety and Clinical Outcomes

Peter Verdonk,<sup>\*†</sup> MD, PhD, Philippe Beaufils,<sup>‡</sup> MD, Johan Bellemans,<sup>§</sup> MD, PhD,  
Patrick Djjan,<sup>||</sup> MD, Eva-Lisa Heinrichs,<sup>||</sup> MD, PhD, Wouter Huysse,<sup>‡</sup> MD,  
Heinz Laprell,<sup>\*\*</sup> MD, Rainer Siebold,<sup>††</sup> MD, PhD, and René Verdonk,<sup>†</sup> MD, PhD

- Safe
- Statistically and clinically significant improvements in all patient outcomes scores at 6, 12 and 24 months
- All efficacy scores continue to improve between 12 and 24 months
- In KOOS the largest improvements are seen in:
  - Sports and Leisure
  - Quality of Life
- Actifit<sup>®</sup> supports tissue ingrowth with meniscus-like characteristics





- Range of motion (bracing)
  - Week 1-2: 0-30°
  - Week 3: 0-60°
  - Week 4-5: 0-90°
  - Week 6: 90 and more
- Walking
  - Week 1-3: non weight bearing
  - Week 4-8: progressive loading
    - 10kg per week for patients weighing  $\geq 60\text{kg}$
    - 15kg per week for patients weighing  $\geq 90\text{kg}$
  - Week 9: full weight bearing

# 24 MONTH F/U FROM EU STUDY COMPLETED

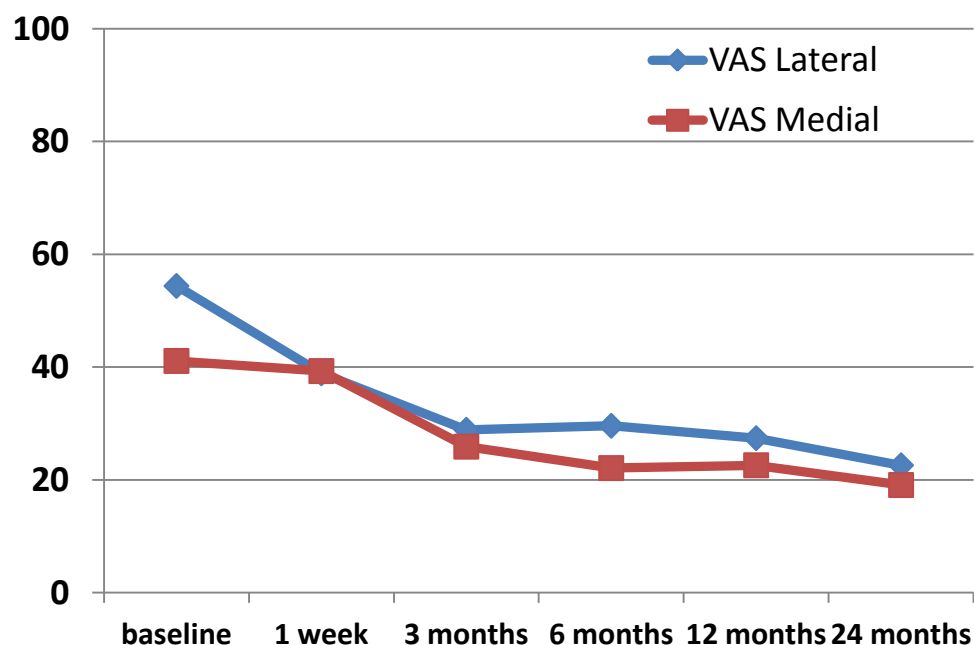


## The Orteq EU Clinical Study Team

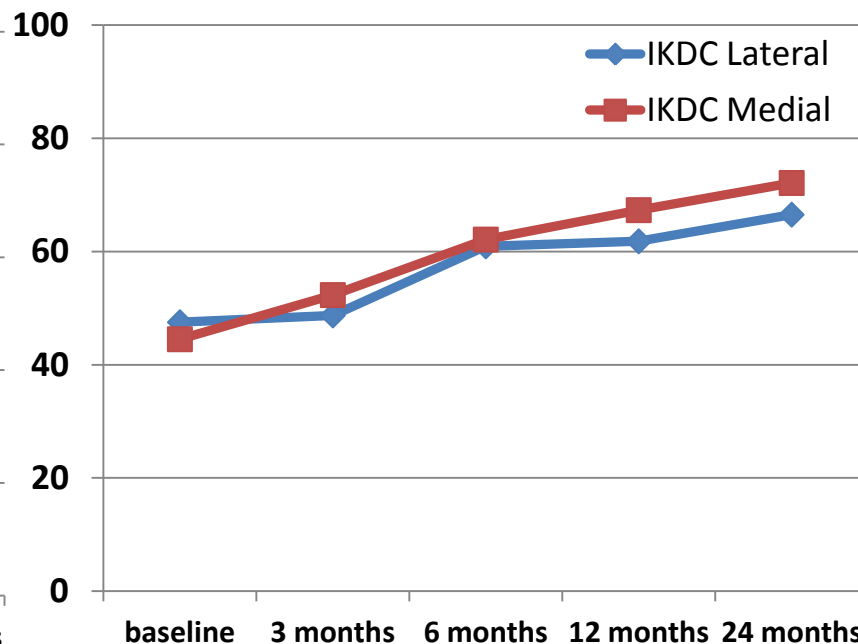
- Prof R Verdonk
- Dr P Beaufile
- Prof P Neyret
- Dr H Paessler
- Dr R Cugat
- Dr P Colombet
- Dr H Laprell
- Dr P Djian
- Prof J Bellemans
- University Hospital Gent
- Centre Hospitalier de Versailles
- Centre Livet de Lyon
- Atos Praxisklinik Heidelberg
- Hospital Quirón de Barcelona
- Clinique de Merignac-Bordeaux
- Lubinus Clinicum of Kiel
- Institut Nollet Paris
- University Hospital Pellenberg

## Statistically and Clinically<sup>‡</sup> Significant Pain Reduction and Functional Improvement

**VAS\***



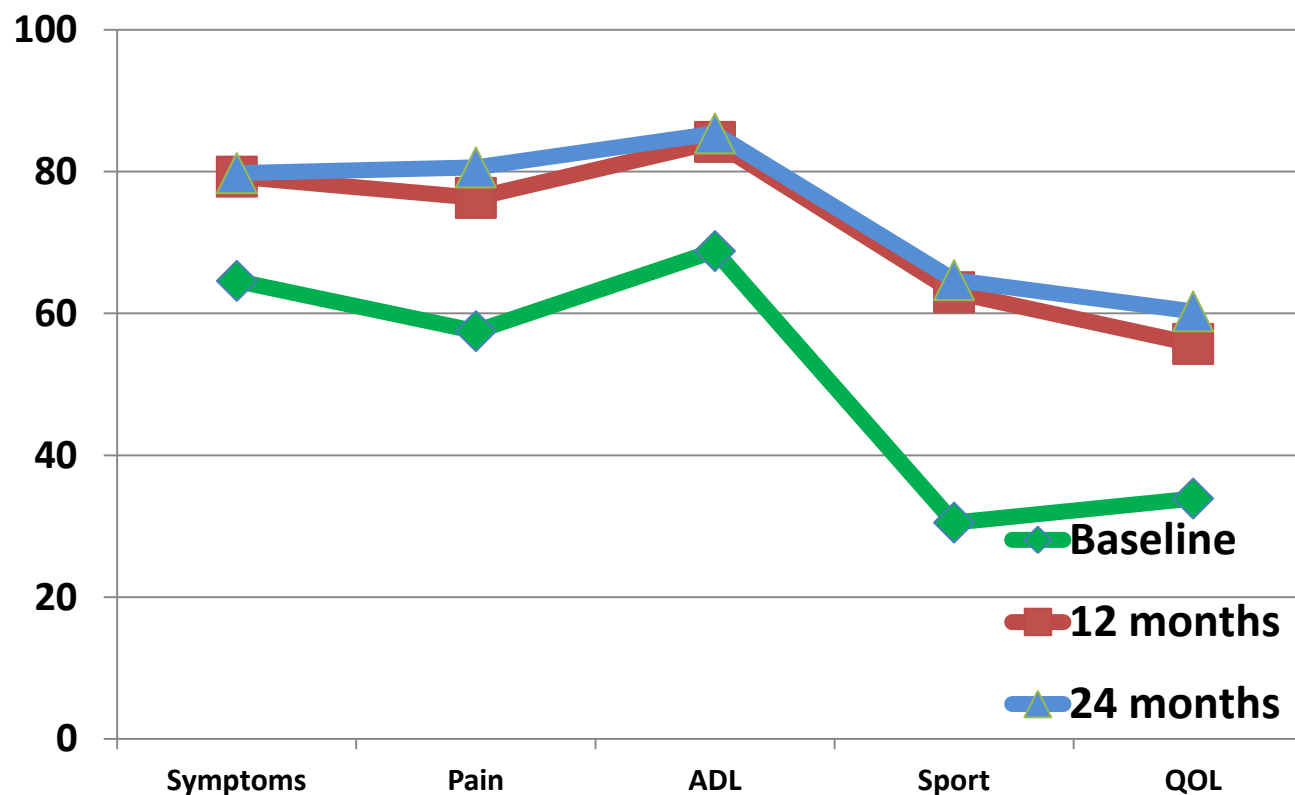
**IKDC\***



\* Mean values ; n= 39 at 24 months (24 medial and 15 lateral)

<sup>‡</sup> Kelly AM. Emerg Med J. 2001  
Irrgang JJ. Am J Sports Med. 2006

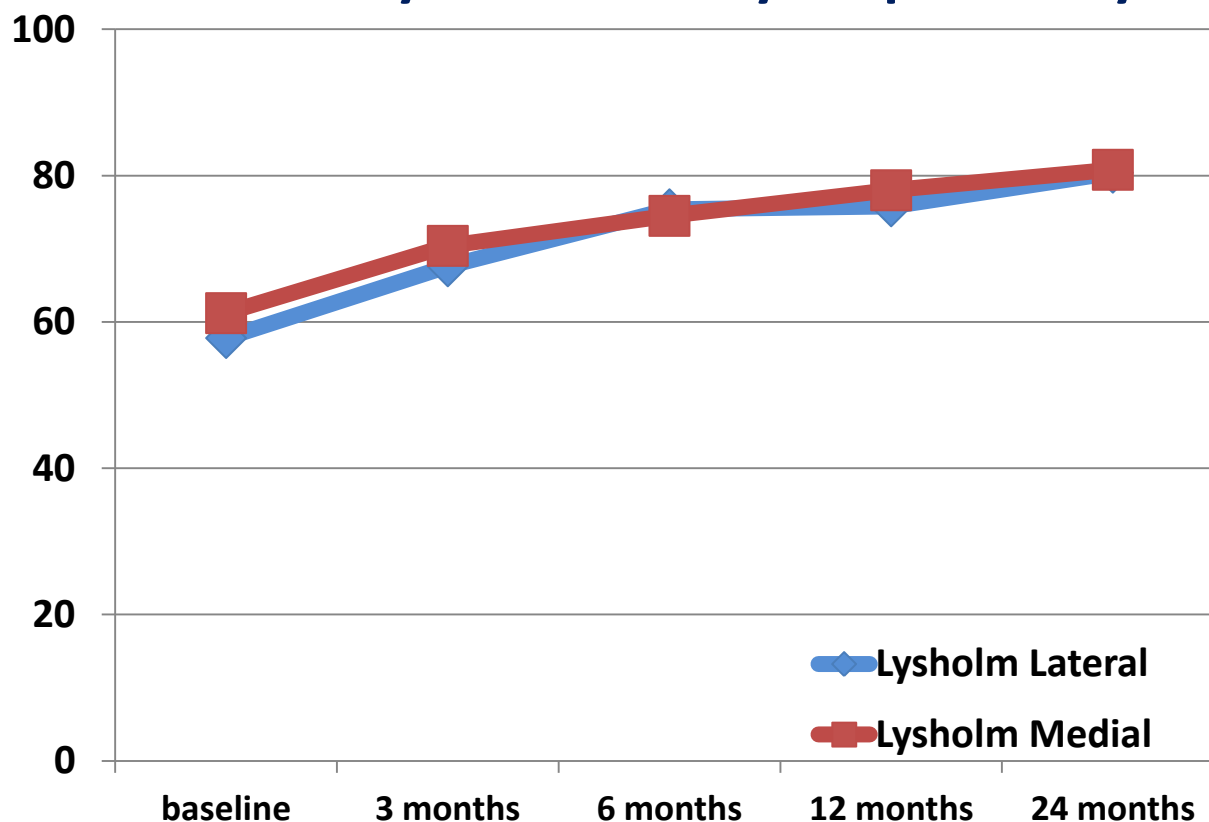
## Statistically and clinically<sup>‡</sup> improved KOOS scores\*



\* Mean values ; n= 39 at 24 months

<sup>‡</sup> Roos EM. Health Qual Life Outcomes. 2003

## Statistically and clinically<sup>‡</sup> improved Lysholm scores\*



<sup>‡</sup> Briggs KK. J Bone Joint Surg Am 2006

\* Mean values ; n= 39 at 24 months (24 medial and 15 lateral)

# MRI RESULTS OVER 24 MONTHS AND HISTOLOGY AT 1 YEAR



## MRI Evaluation

- ☐ Stable or improved cartilage scores in all cases in the index area
- ☐ 7 with improved cartilage scores!!
- ☐ Any deterioration related directly to pre-existing conditions

## HISTOLOGY

- ☐ Full biocompatibility (no cell death, necrosis, inflammatory reaction) in the biopsy samples
- ☐ No evidence of long-term capsule inflammation

# EU PILOT STUDY PARAMETERS



## Safety Confirmed at 12, 24 and 36 months

- ☐ Arthroscopic Relook at 12 months !!
- ☐ Device stability and cartilage score on MRI (1w, 3,12, 24, 36 months)

## Performance and Efficacy

- ☐ Tissue ingrowth
  - Dynamic Contrast Enhanced MRI (3 months)
  - Tissue Biopsy (12 months) !!!
- ☐ Pain
  - VAS (Baseline, 1 week, 3, 6, 12, 24 months)
- ☐ Functionality
  - IKDC, Lysholm, KOOS (Baseline, 3, 6, 12, 24 months)