



UMC Utrecht



# Gebruik van Fitrix voor kraakbeenherstel

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University Medical Center Utrecht

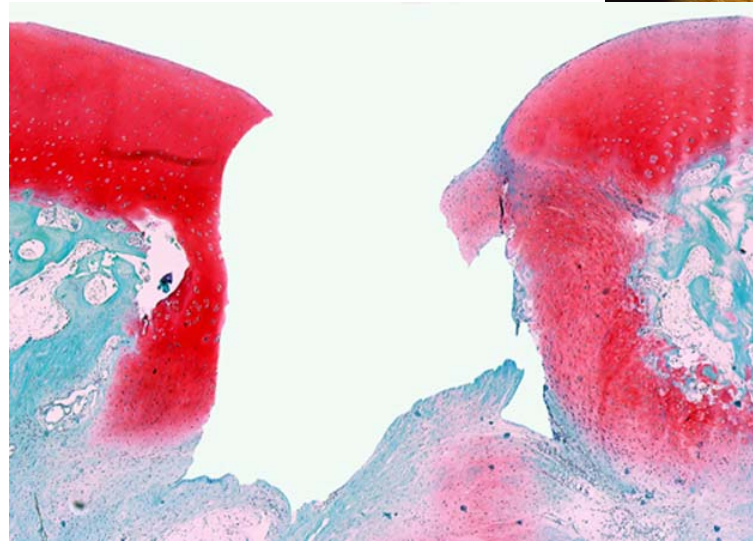
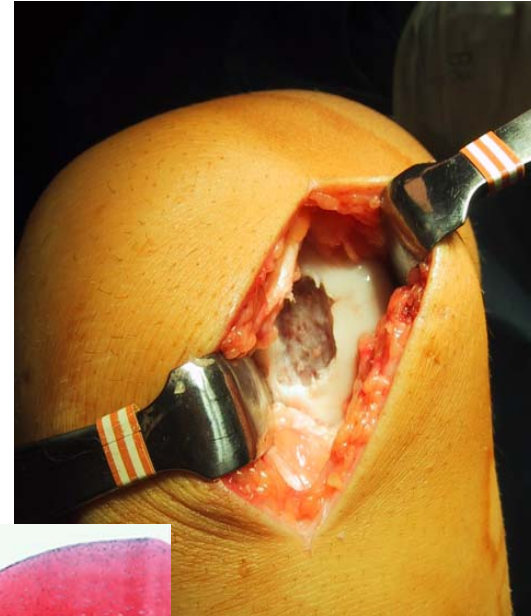
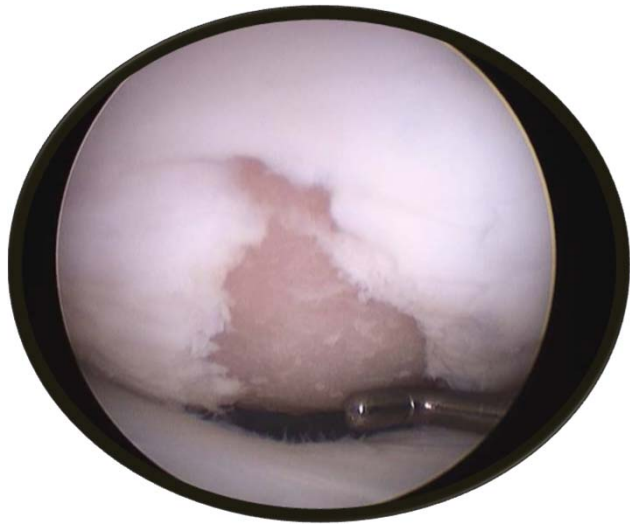
# Disclosures

None related to this topic

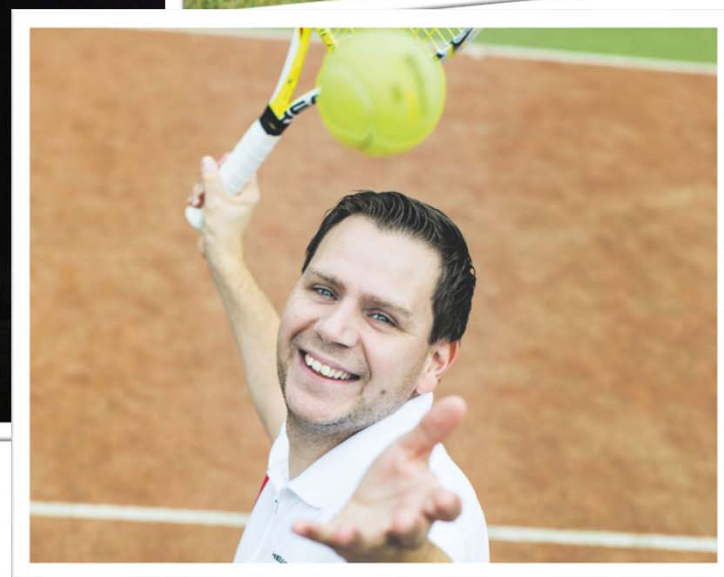
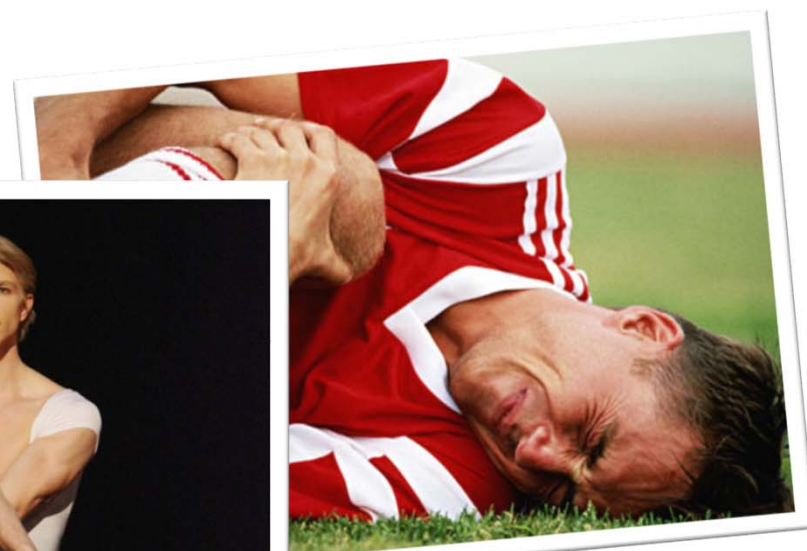
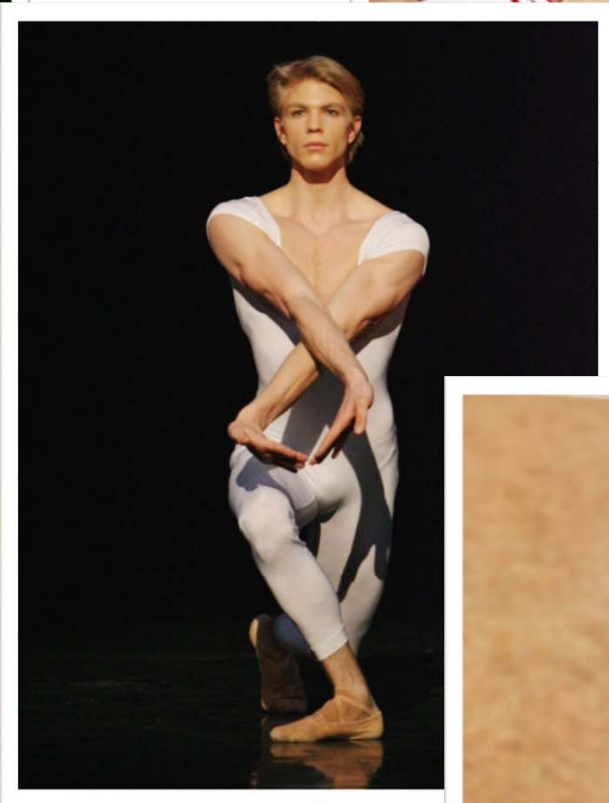
IMPACT is investigator–driven without commercial involvement



# Kraakbeen defecten

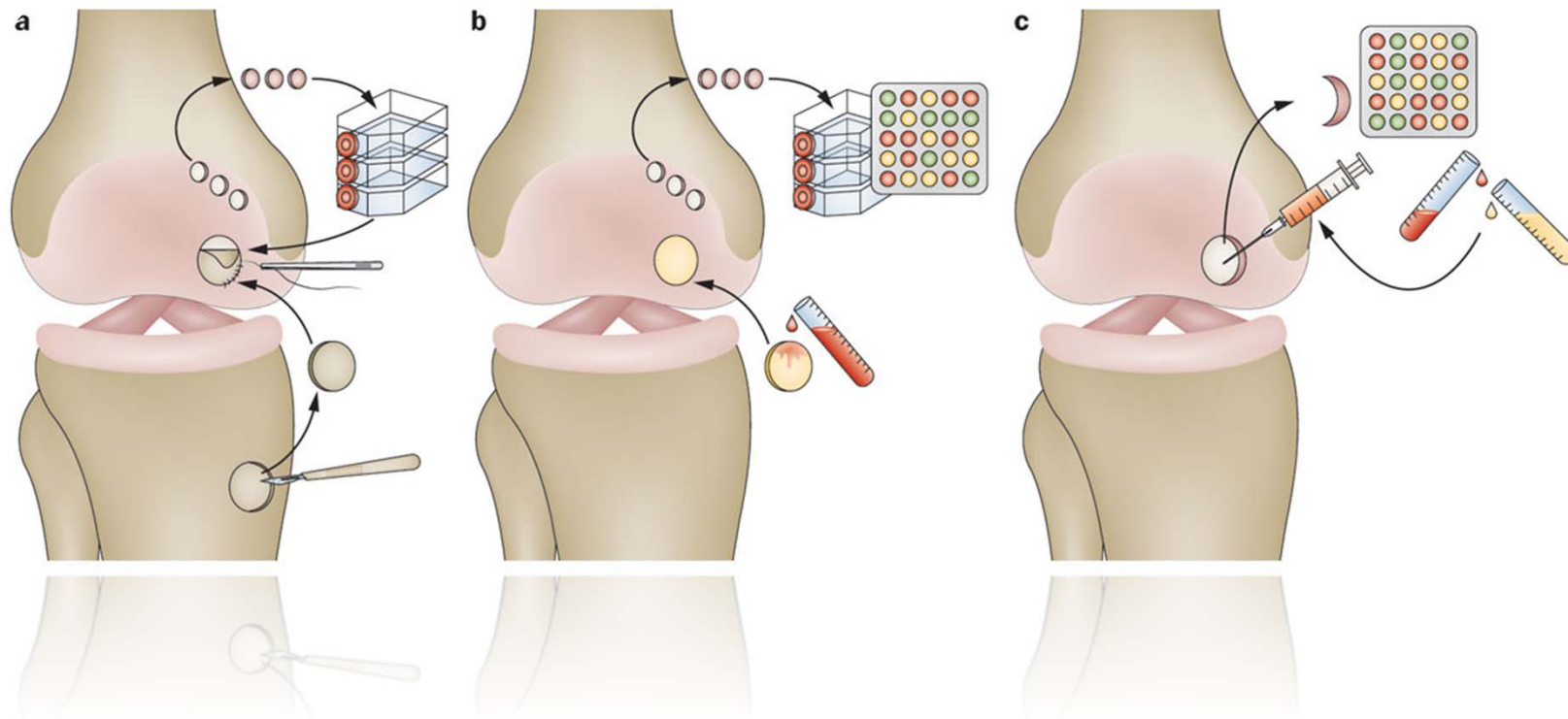


# De patiënten

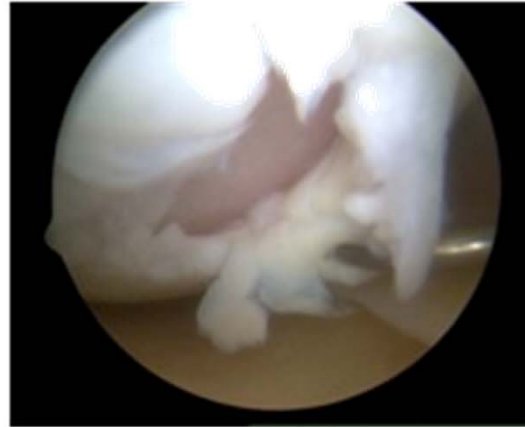


# Autologe kraakbeencel transplantatie (ACI)

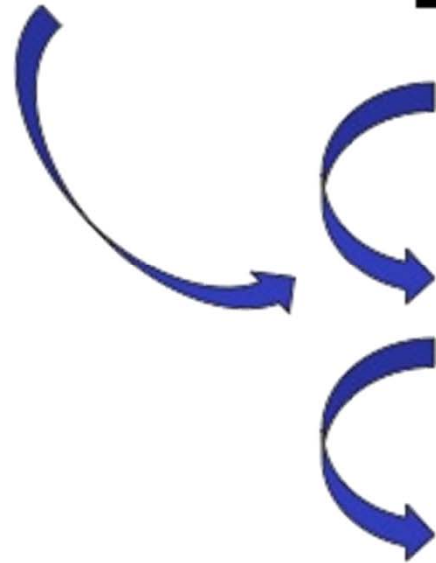
- MACI (Genzyme / Sanofi)
- ChondroCelect (TiGenix)



# Eén-staps procedure



One surgery

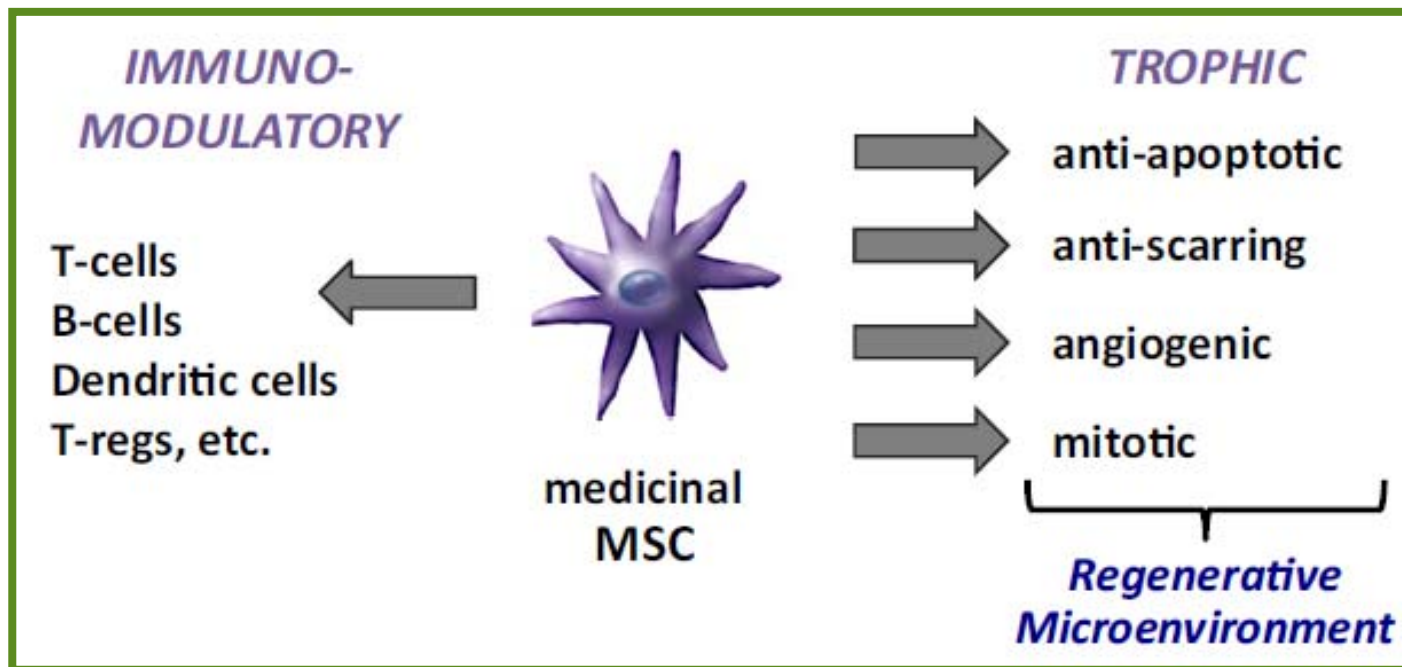
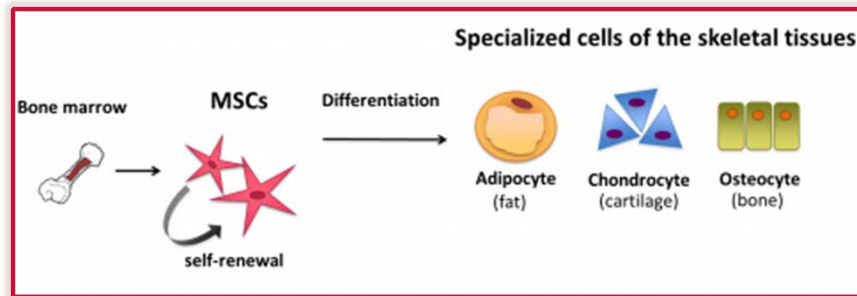


Isolate, wash and **mix** cells

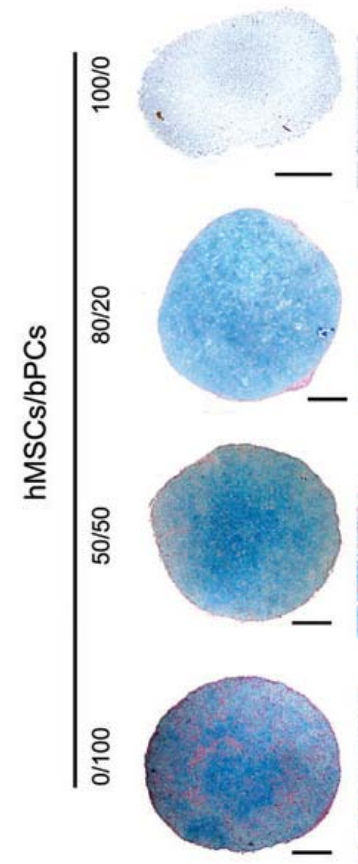
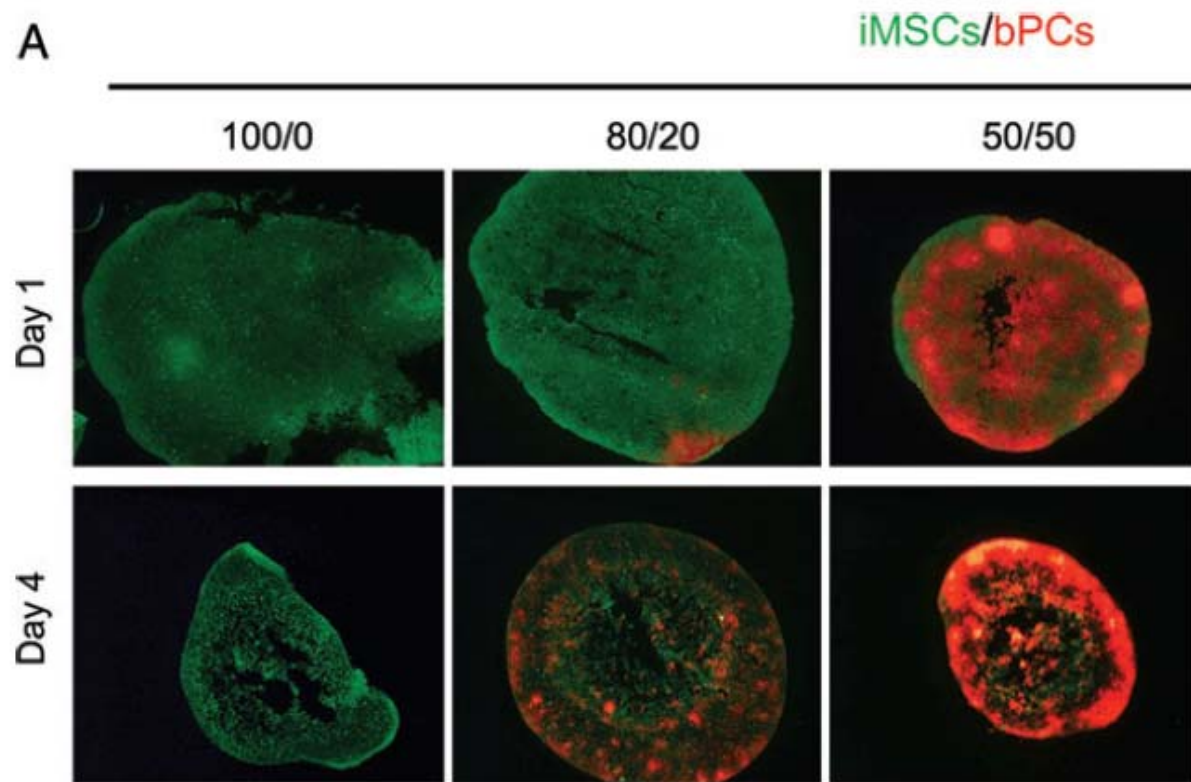
Implant cells  
in fibrin glue



# Allogene mesenchymale stromale cellen (MSCs)

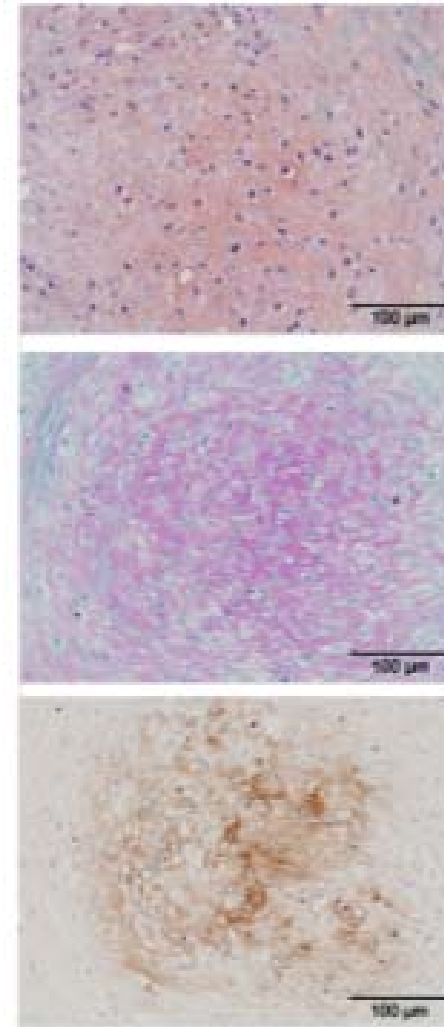
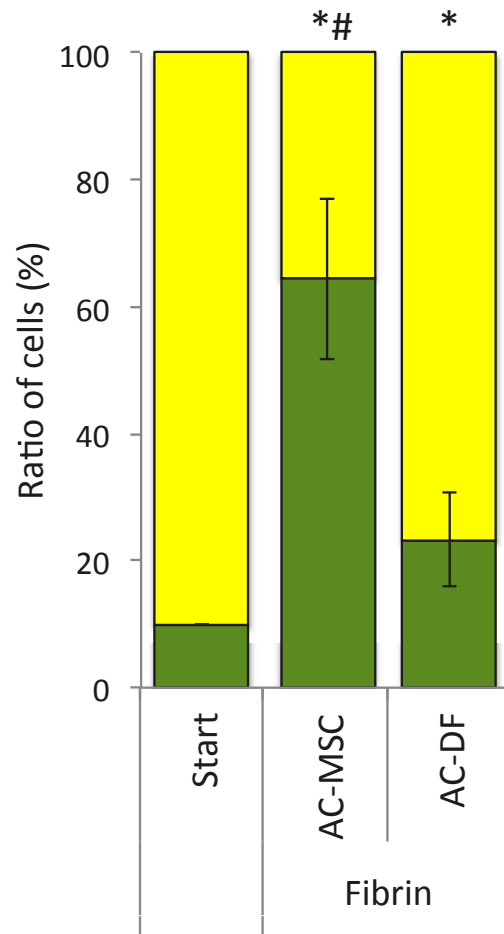


# Chondroinductie





# Chondroinductie primaire cellen in fibrine



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Instant Allogeneic MSC Product  
accompanying  
Autologous Chondron Transplantation



## Fase I / II studie

- 35 patiënten (24 man, 11 vrouw)
- Defect grootte 3,2 ( $\pm$  0,7) cm<sup>2</sup>
- Stabiele knie met functionele meniscus
- Geen gewrichtsslijtage of ontsteking in de knie

### Uitkomstmaten:

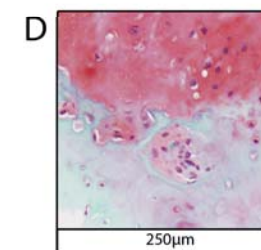
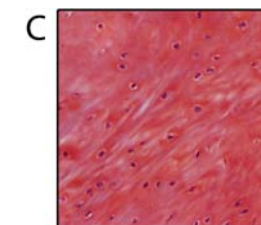
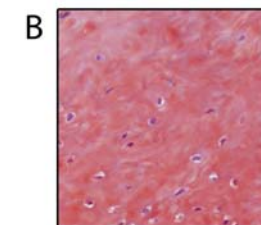
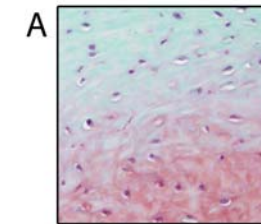
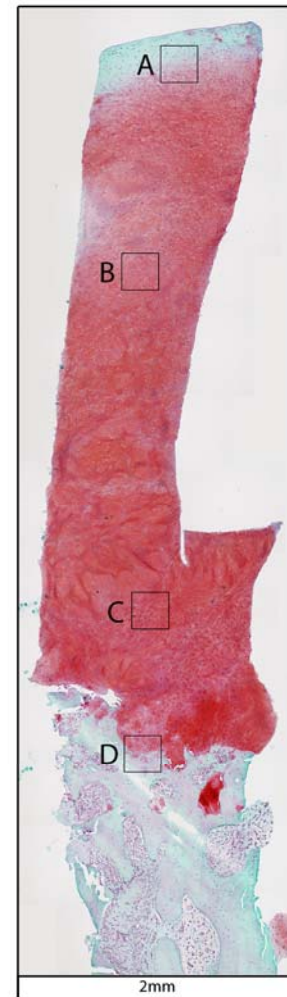
- Veiligheidsdata (bijwerkingen)
- Klinische uitkomst (vragenlijsten)
- MRI
- **Biopten (histologie en DNA analyse)**



## Kijkoperatie na 1 jaar



# Biopt: histologie & DNA analyse



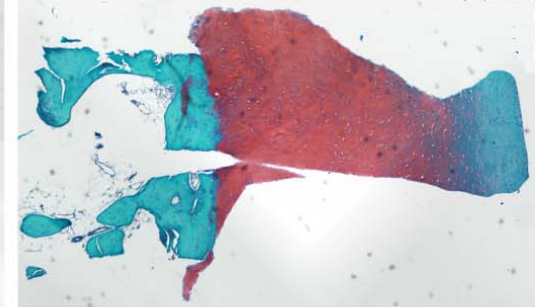
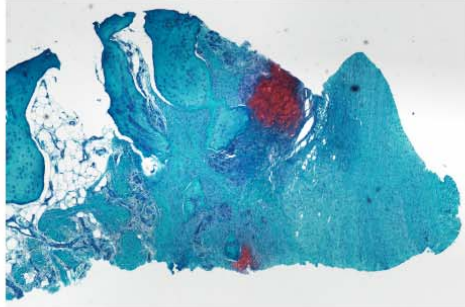
# Biopt: histologie 32 patienten

Worst N = 3

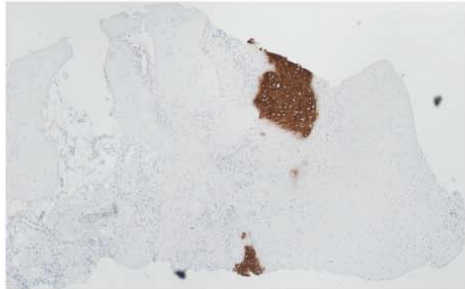
Mean N = 20

Best N = 9

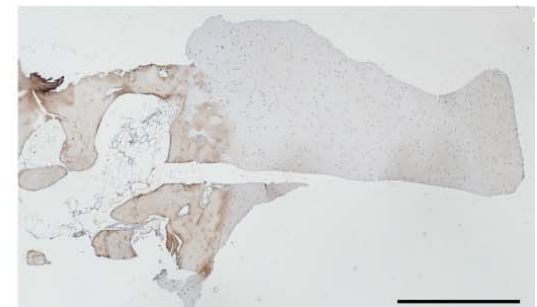
Saf O



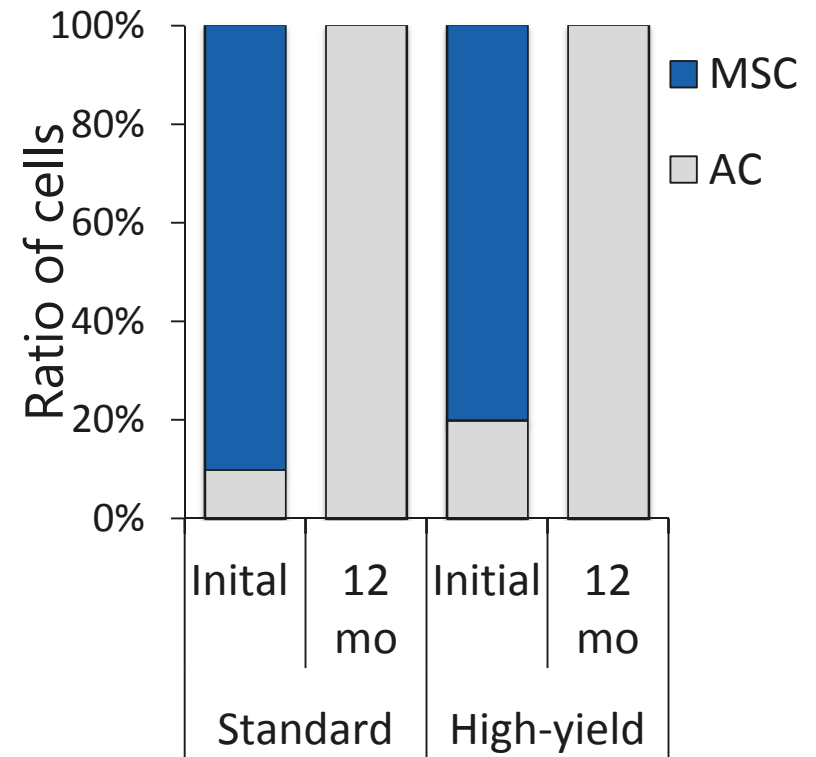
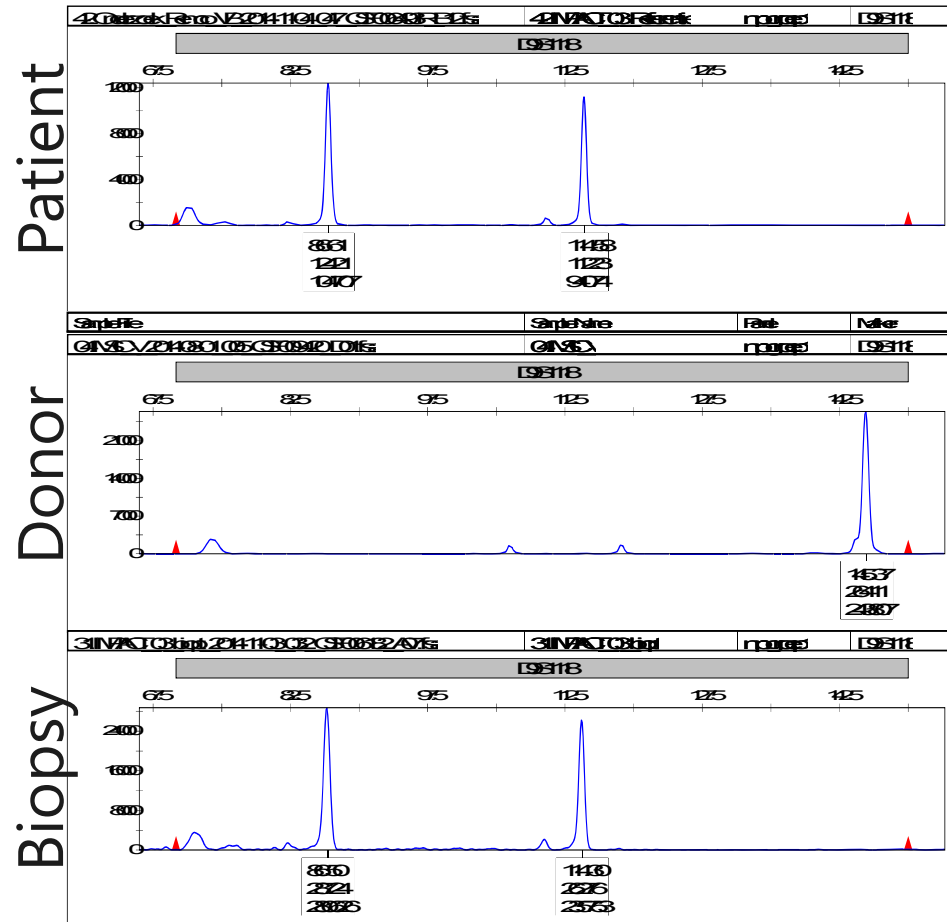
Coll II



Coll I



# Biopt: DNA analyse



80% - 90% allogene MSCs stimuleren 100% autoloog herstel  
weefsel



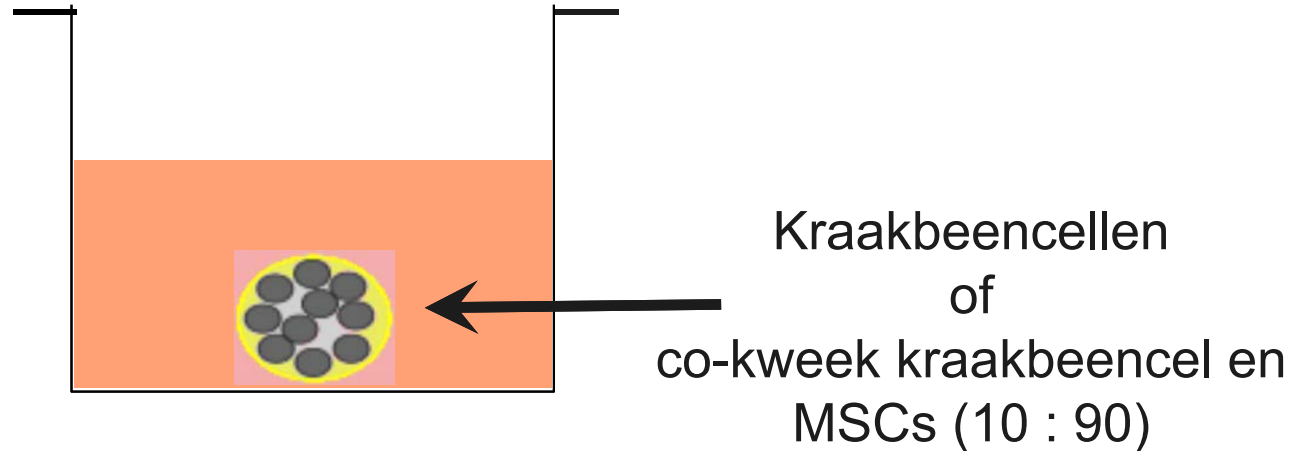
## Doel

Om te onderzoeken of Fitrix weefsellijm als alternatief voor de andere fibrine weefsellijmen (Beriplast, Tisseel) gebruikt kan worden





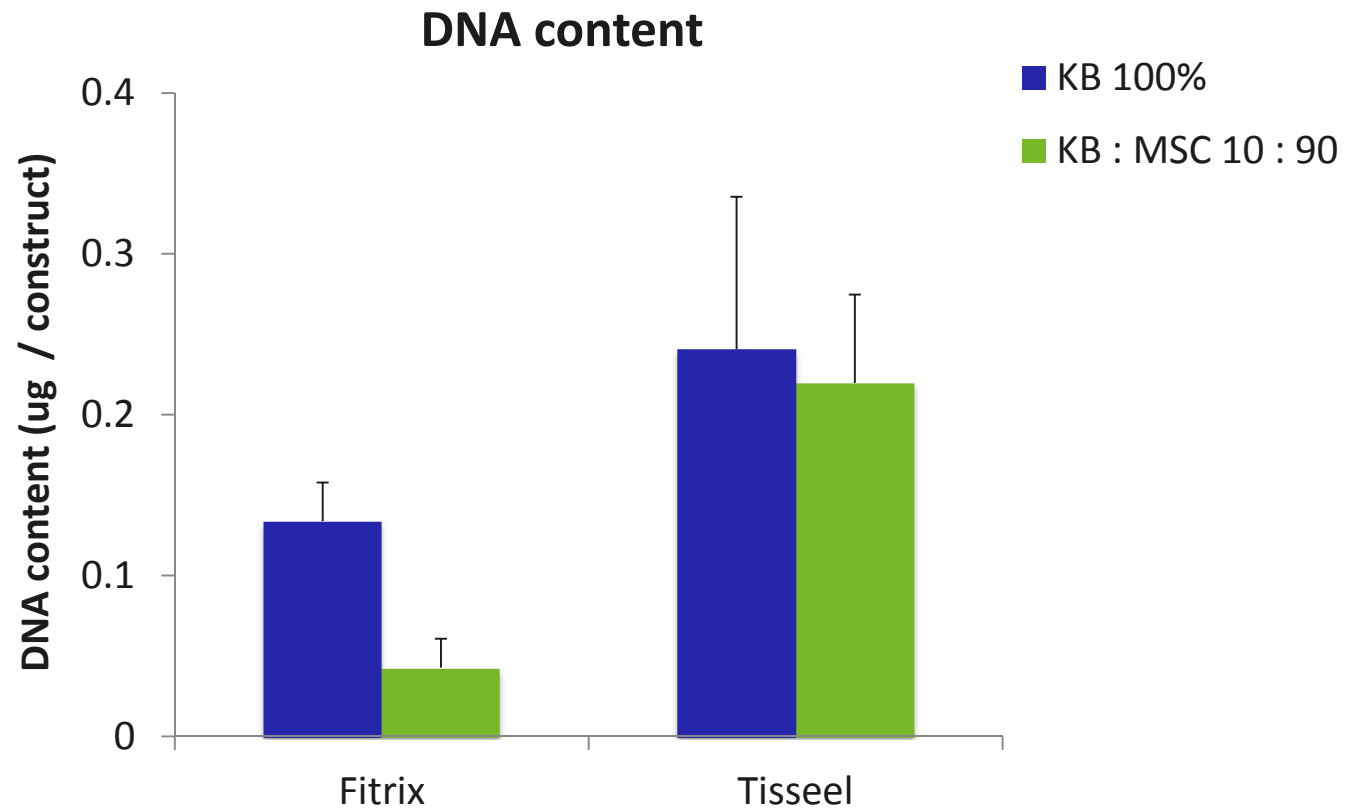
## Materiaal & methode



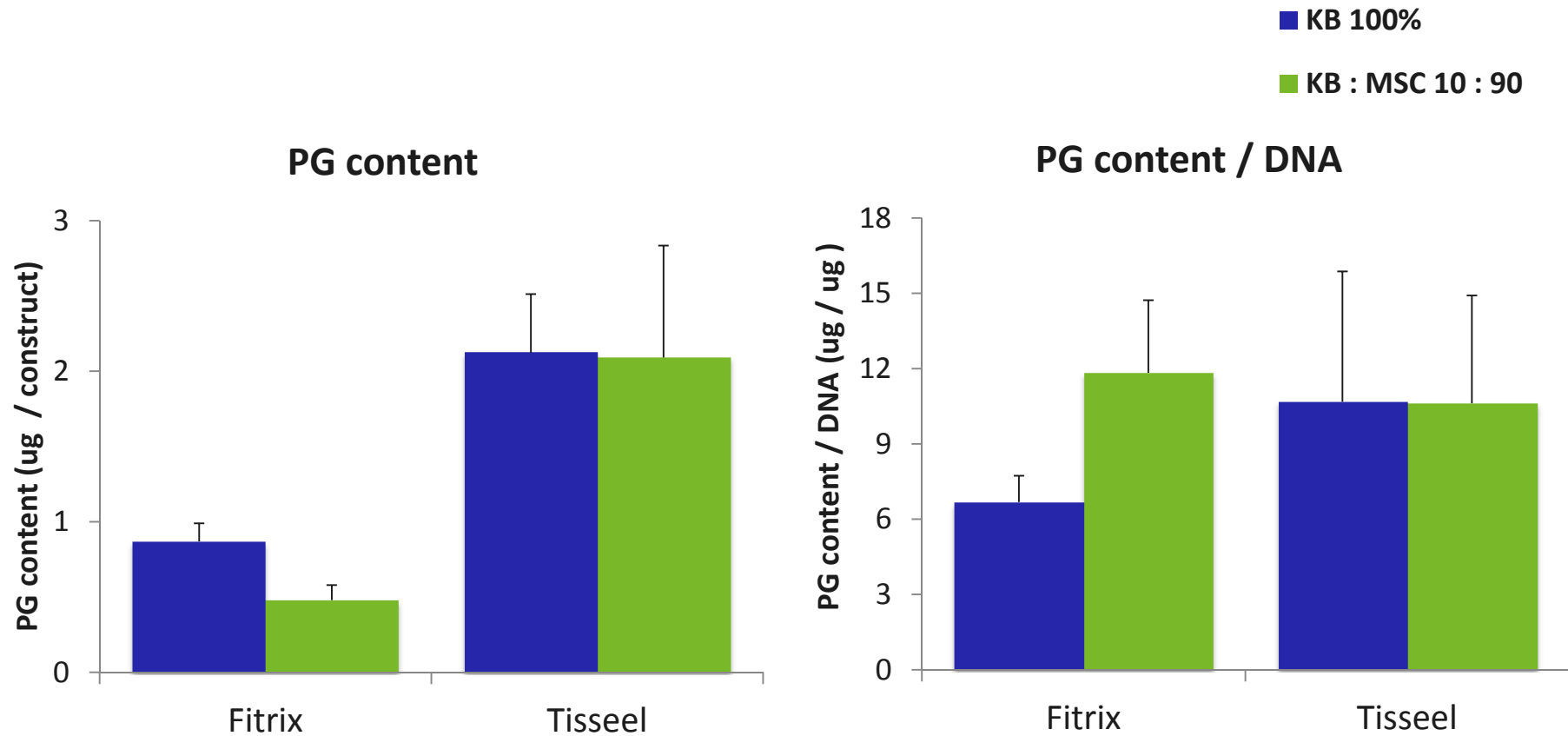
- In fibrine weefselijm
- Kweektijd van 28 dagen
- Productie van kraakbeencomponenten (proteoglycanen en collageen)
- Ratio kraakbeen cellen : MSCs



# DNA content (~ aantal cellen)



# Proteoglycanen (PG) productie

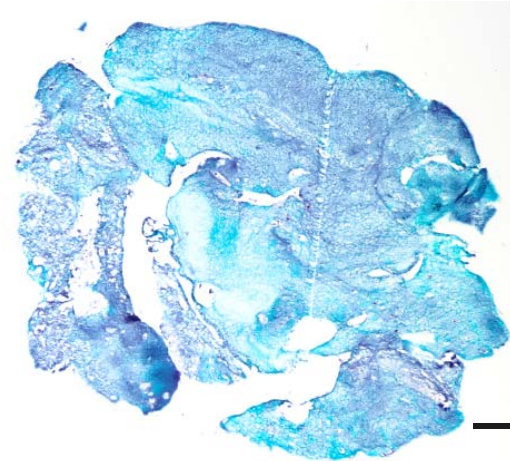
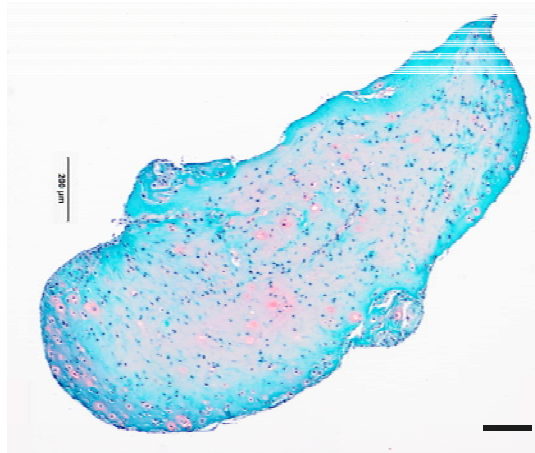


# Histologie - proteoglycanen

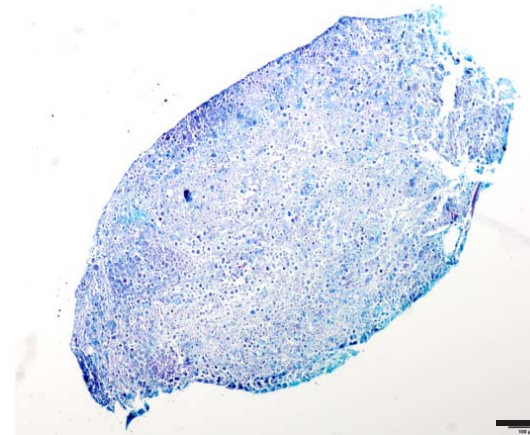
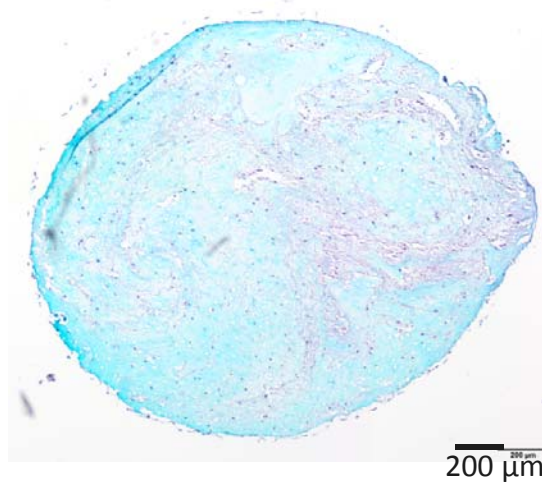
Tisseel

Fitrix

100% KB



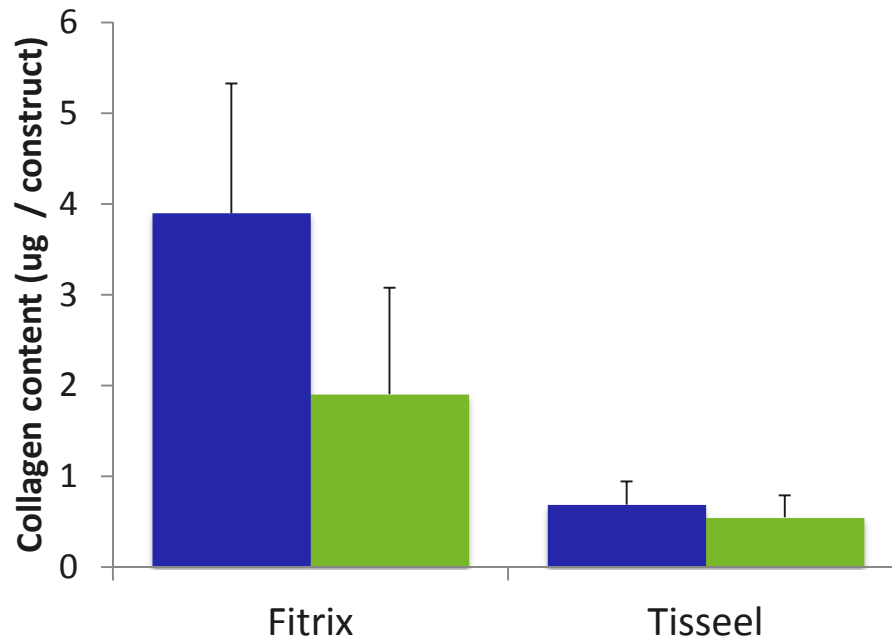
10 : 90  
KB : MSC



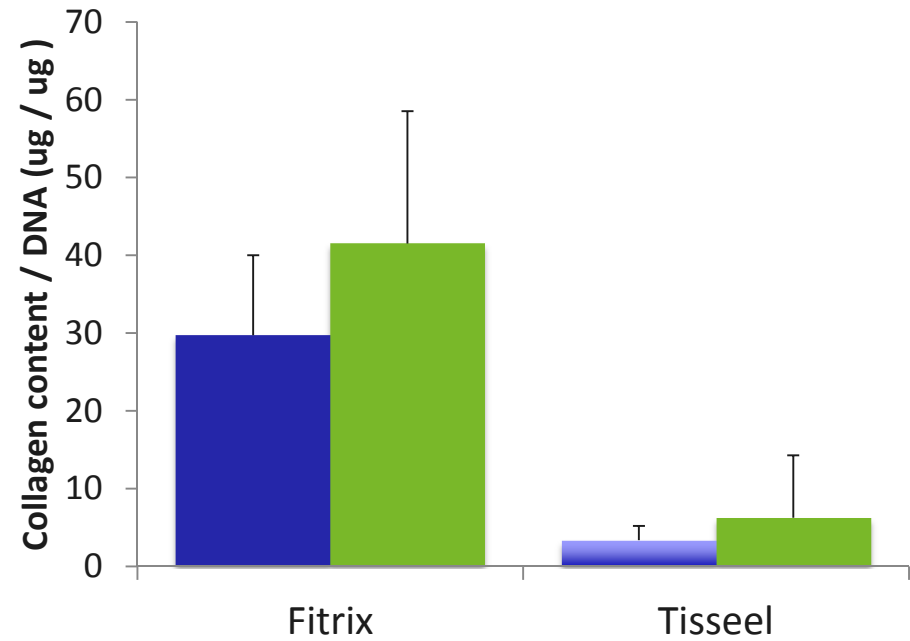
# Totaal collageen productie

■ KB 100%  
■ KB : MSC 10 : 90

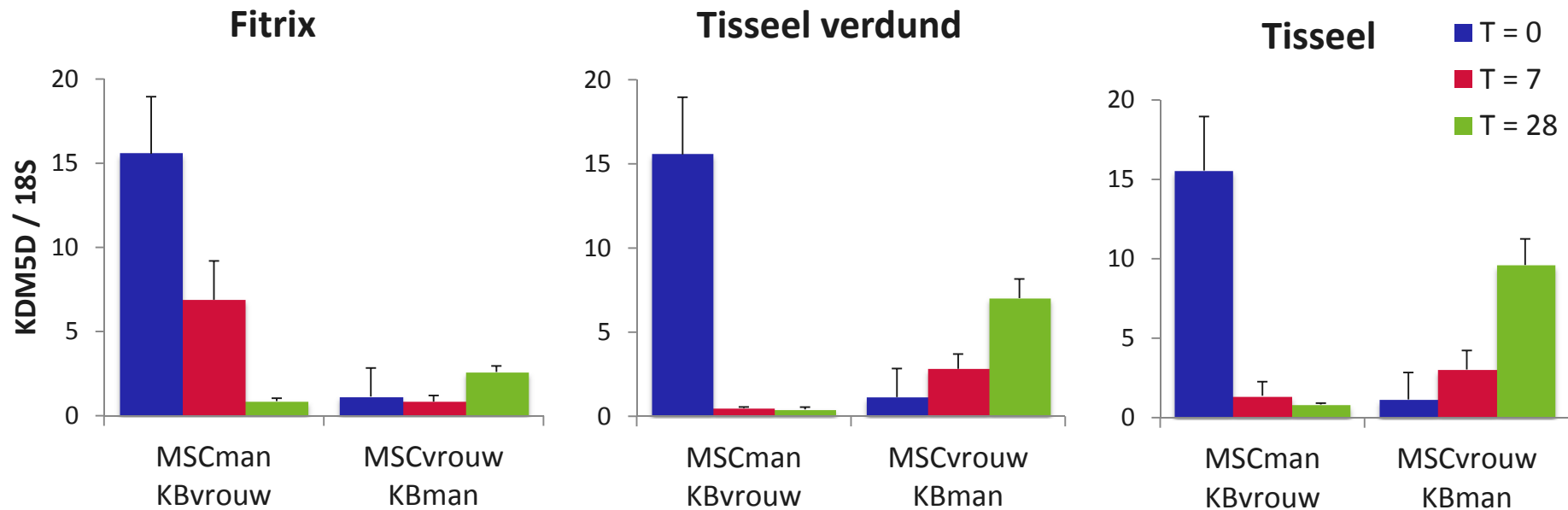
### Collagen content



### Collagen content / DNA



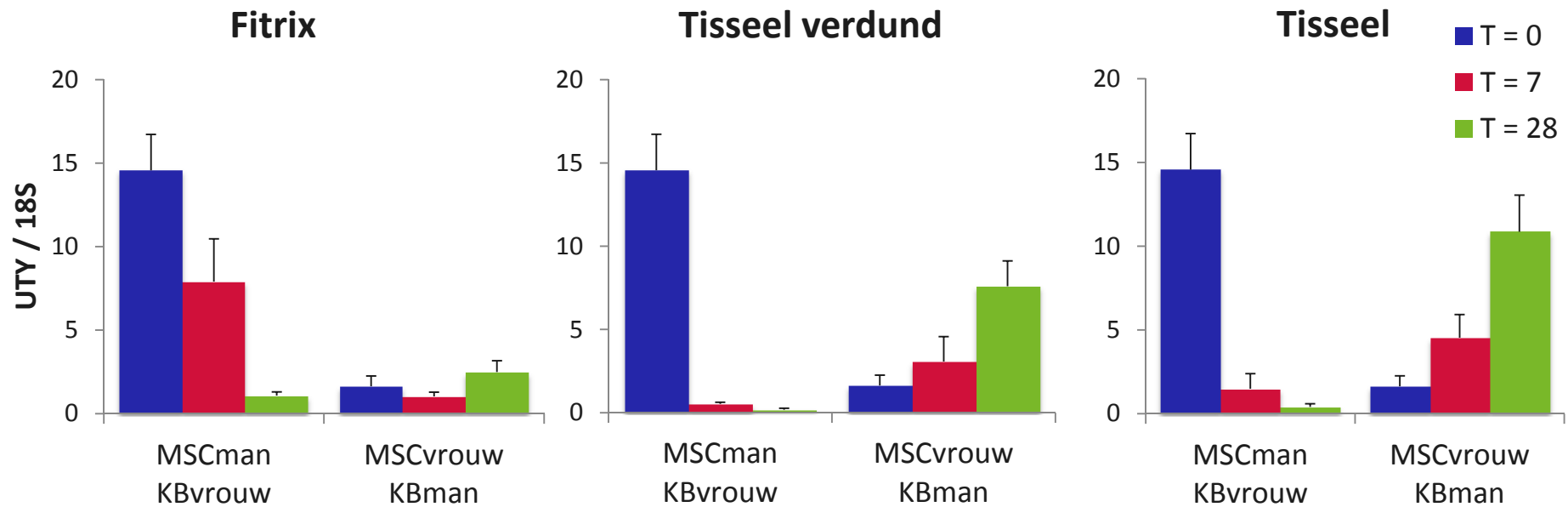
# Ratio kraakbeencil : MSCs



KDM5D is een Y-chromosomaal gen



# Ratio kraakbeencil : MSCs



UTY is een Y-chromosomaal gen



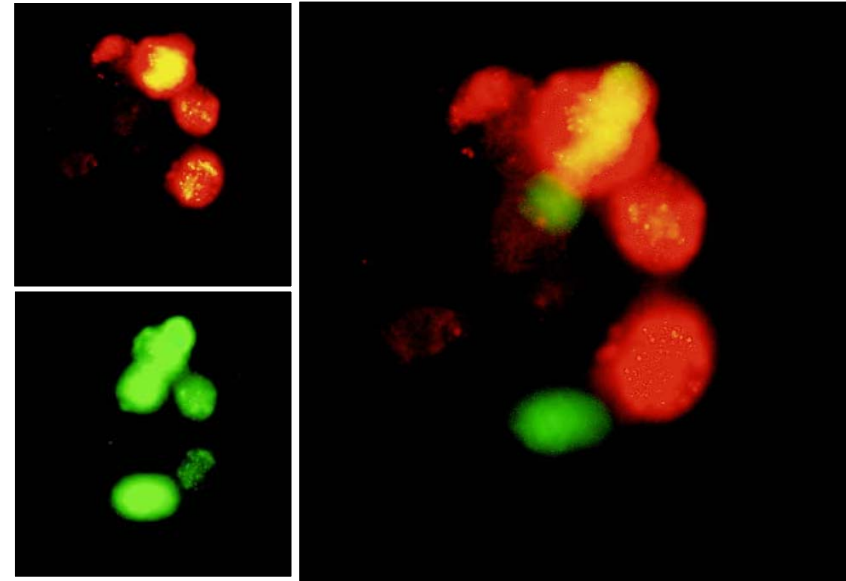
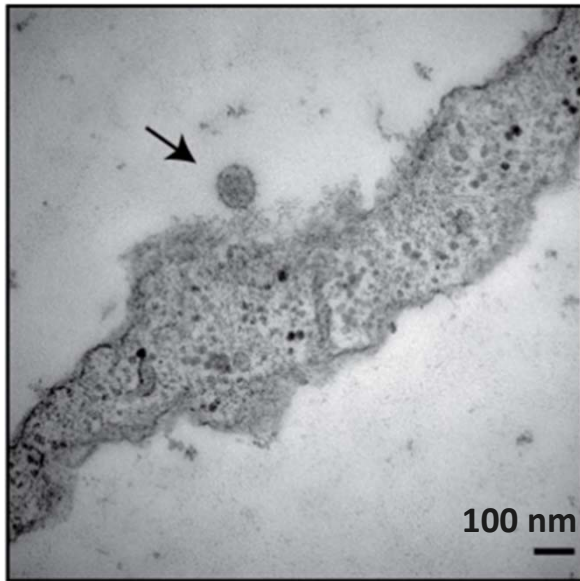
## Conclusie & discussie

- De totale hoeveelheid cellen is na 4 weken kweek verlaagd in Fitrix. Hoewel de MSCs in eerste instantie langzamer verdwijnen, zet dit juist niet aan tot proliferatie van de kraakbeencellen.
- Kraakbeencellen en cokweken van kraakbeencellen en MSCs produceren proteoglycanen in Fitrix. De absolute hoeveelheid is wel iets lager dan in Tisseel.
- De totale collageen productie van kraakbeencellen en cokweken van kraakbeencellen en MSCs is hoger in Fitrix dan in Tisseel.
- Fitrix lijkt een fibrine waarin MSCs langer overleven, echter mist hierdoor de chondroinductie.
- Ondervinden de cellen minder stress?

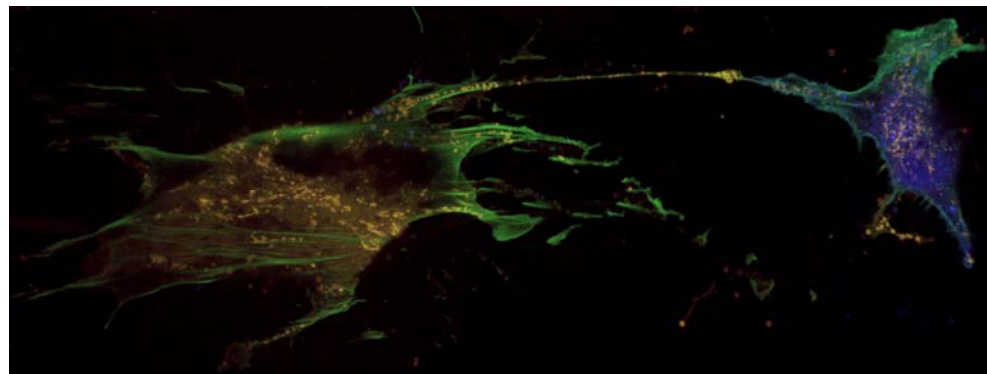




## Intercellulaire communicatie – stress?



Calcein-AM / DiI MSCs



## Special thanks to:

- Koen Dijkstra
- Tommy de Windt
- Roel de Weger
- Ineke Slaper-Cortenbach
- Daniel Saris
- Marga van Hulst-Sundermeijer
- Henry Kuper
- Dirk de Korte



**imp|Act.**



**ZonMw**

