



Drug delivery in NL

Plus an overview on hydrogel technology from
InGell and OncoLize

Mike de Leeuw

Life Sciences and Health event, Oss,
22 November 2017

Mike G.W. de Leeuw - Founder



Founder OncoLize, InGell Labs and Branching Tree BV

Founder DSM Biomedical

Initiator BMM – Program

Interim positions in biotech, cell therapy and med devices

DSM China/India/Europe

SHELL Biotech

Unilever b-2-b product management

Tumour virology and business administration

www.linkedin.com/in/mikedeleeuw

Disclaimer - stimulator

I have been asked to present a short overview of prominent people and organizations active in polymer-enabled drug delivery in the Netherlands, and what it is I have been doing in this field.

The following slides are intended to be informative, and it is neither complete nor judgemental.

Discuss, add, network!

mike@branchingtree.com

BioMedical Polymers in NL: two nestors

Prof Jan Feijen – University of Twente

- Block-co-polymers
- Hydrogels, drug delivery, tissue engineering

Prof Albert Pennings – University of Groningen

- Poly-lactic acid
- Implants, microspheres

The next generation of medical polymer creators...

Piet Lemstra in Technical University Eindhoven

- Trigger-sensitive polymers
- Fiber technology

Wim Hennink – Univ. Utrecht

- Nanostructures
- Drug delivery
- Gene and particle delivery

Dirk Grijpma – Univ Twente and Univ. Groningen

- Implants, scaffolds, coatings

Biomedical polymers Innovators

Company	Location	Brand	Uses	Available
Organon	Oss	Implanon	Drug delivery	1998
		Nuva Ring	Drug delivery	2001
DSM Dyneema	Geleen	Dyneema purity	Implants	2010
Isotis	Bilthoven	PolyActive	Tissue engineering	2004
OctoPlus	Leiden	PolyActive	Drug delivery	2005
InnoCore	Groningen	SynBiosys	Drug delivery	2006
2-BBB	Leiden	2-BBB	Drug delivery	2008
EmulTech	Eindhoven	EmulTech	Drug delivery	2009
InGell	Groningen	InGell	Drug delivery	2010
Crystal Therapeutics	Maastricht	Cri-Pec	Drug delivery	2013
Hy2Care	Twente	Hy2Care	Tissue engineering	2015

Various forms of drug delivery

Form	Release	Delivery	Companies	Examples
Microspheres	Sustained Localized	Local	InnoCore, DSM	Osteo Arthritis
Implants	Sustained Localized	Local	InnoCore	Hormone therapy
Liposomes	Cross barriers	Circulation	2-BBB	Brain diseases
Hydrogels	Sustained Localized	Local	InGell Labs	Diabetes Osteo Arthritis CNS
Nano-particles	Sustained	Circulation	Crystal Therapeutics	Solid tumors

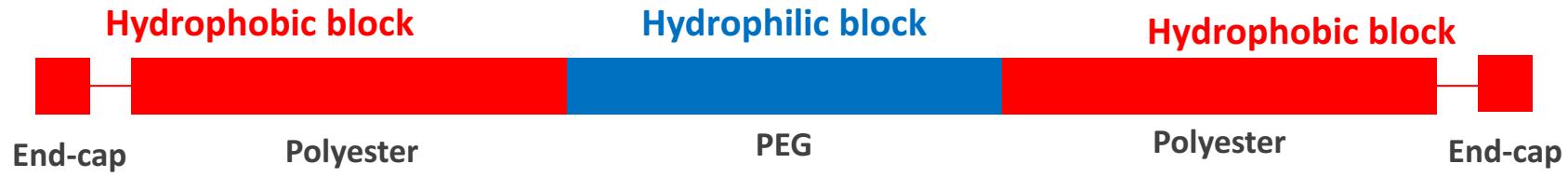


HydroGels for drug delivery

InGell Labs - Groningen



InGell® Architecture



Platform	Total Mw	End-cap	PEG-block	Polyester block- ratio: p-Caprolactone & p-lactide
InGell® Gamma	4500-5500	C2-C6	1200-2000	1.6-2.4
InGell® LQP	1200-2000	C2-C6	200-600	Variable

How? InGell® Injectable drug depots

Injectable formulation



Stable gel depot containing drugs



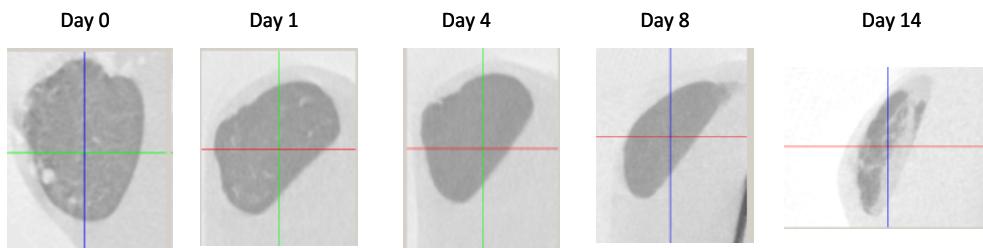
Mix the drug with polymer



Inject with thin needle



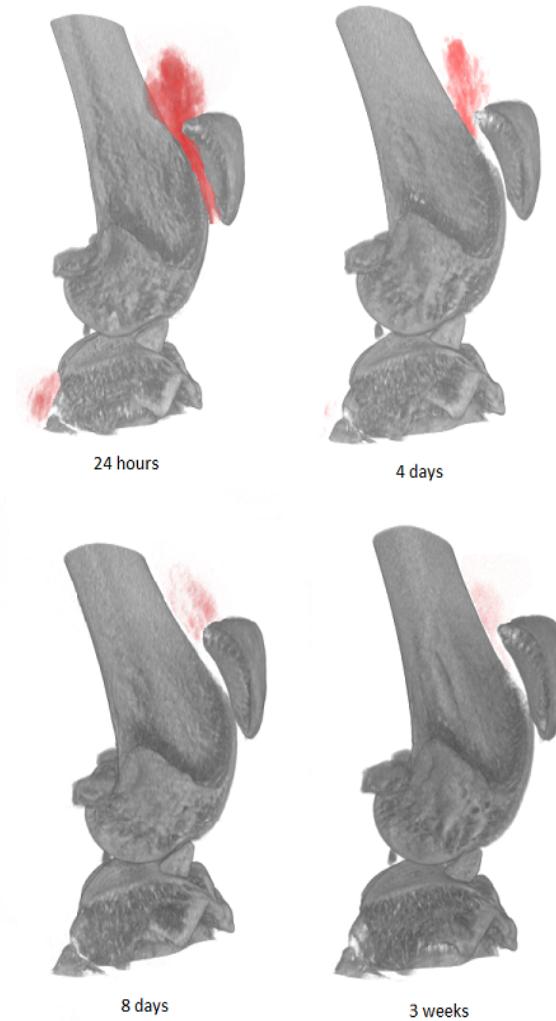
Soft, flexible drug depot
'in situ – in seconds'



Slow, local release of drug,
total degradation of the depot

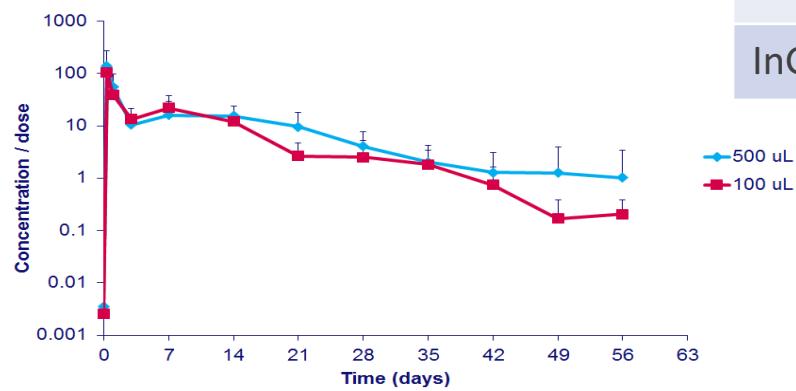
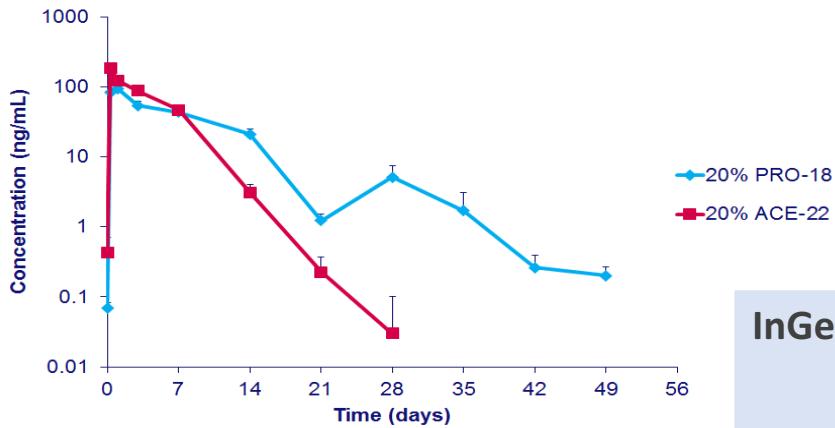
InGell Gamma depots degrade and release gradually in the knee

(M.Sandker et al 2013)



In vivo s.c. depot release of Celecoxib

(P. van Midwoud *et al*, in preparation)



InGell® Depot	Dose	Drug elimination from serum (T1/2)	Delivery Duration
Bolus	10 mg/ml	5 hours	<1 day
InGell Gamma	10 mg/ml	7 days	8 weeks
InGell Gamma	50 mg/ml	10.5 days	8 weeks

InGell® in large animals



Universiteit Utrecht

11/27/17

27-11-17

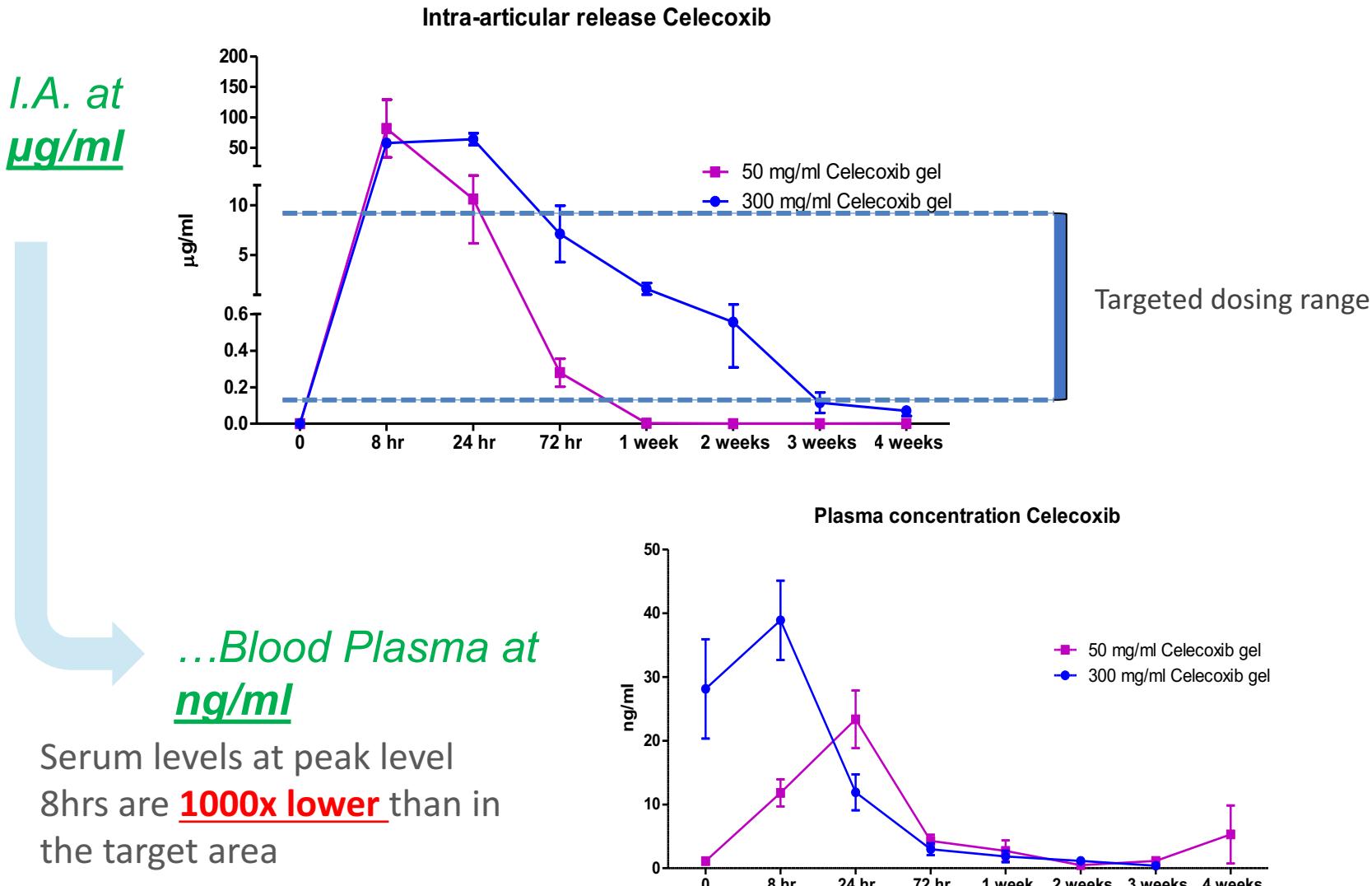
InGell Labs - Copyright 2016

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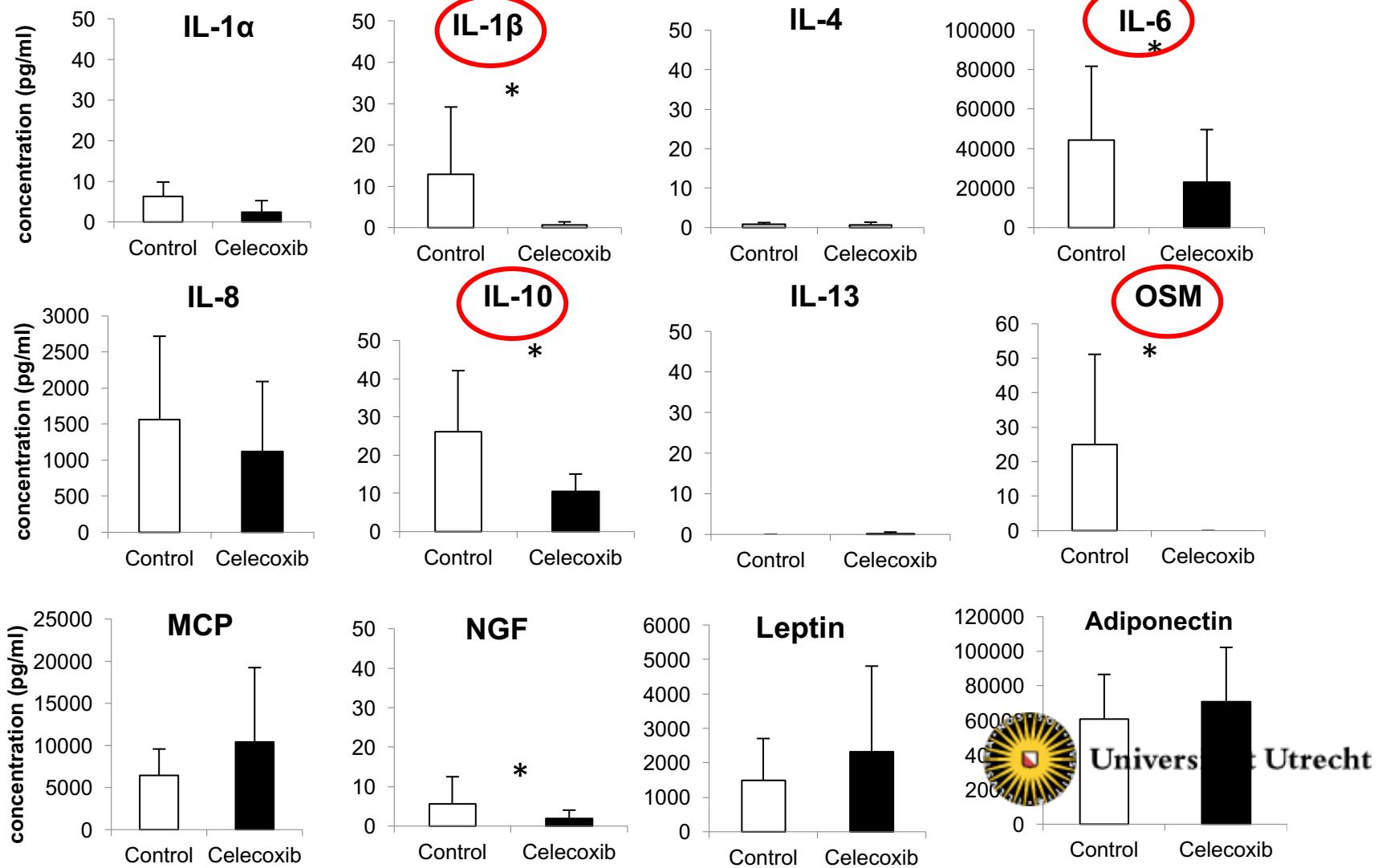
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Sustained release...Localized release

In vivo horse study - Petit et al. Biomaterials (2015)

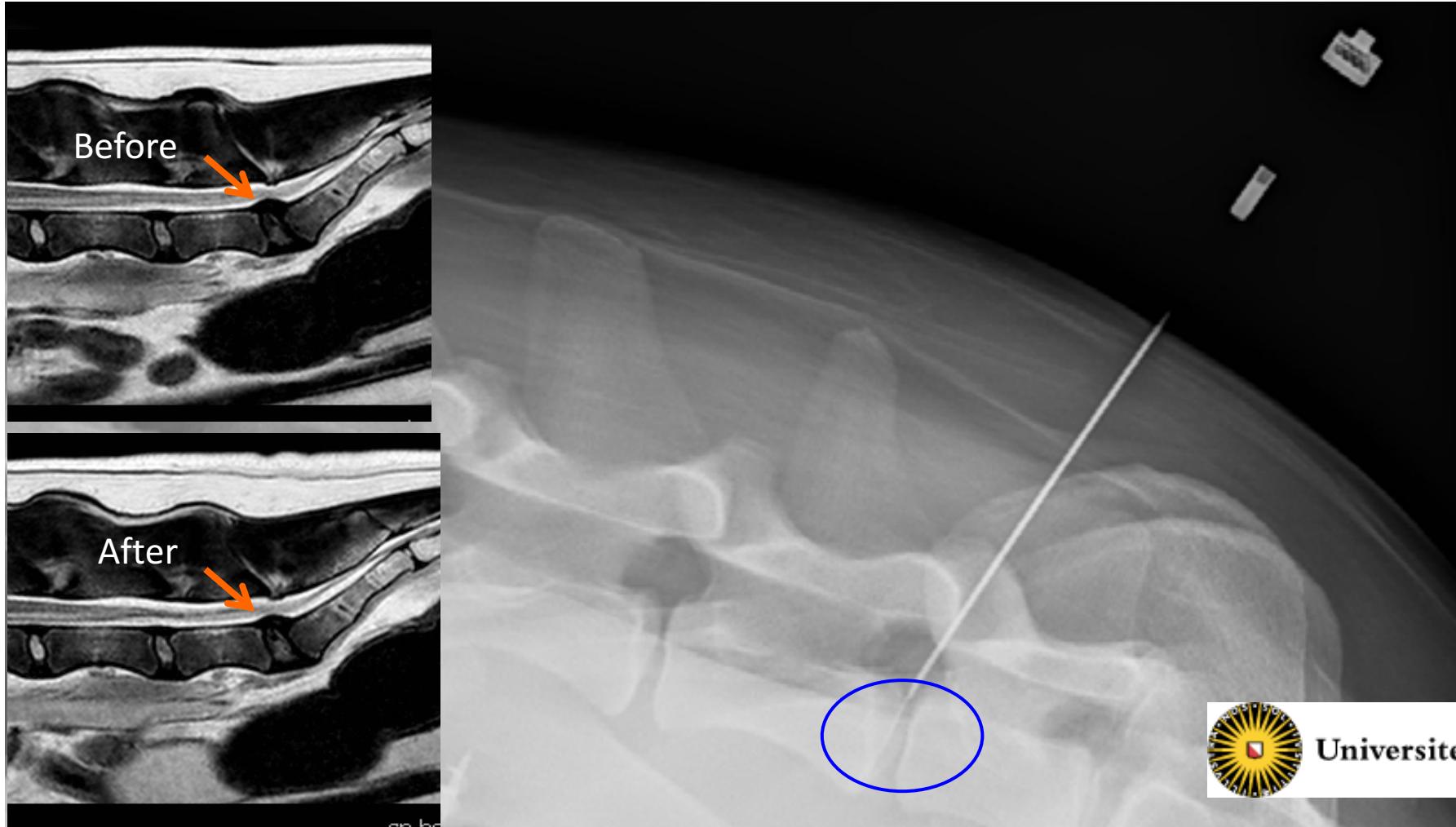


InGell-Celecoxib: suppression of pro-inflammatory markers in co-culture of synovial and cartilage cells (induced by TNF- α)



Percutaneous Intra Vertebral Disc injection (L7-S1)

15cm/27G Hamilton-injector through 20G lead



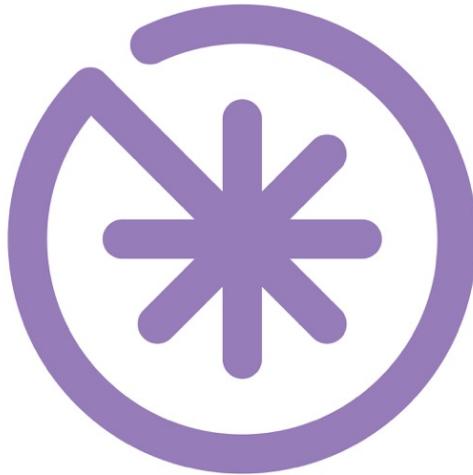
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Clinical study in dog patients suffering from Lower Back Pain

10 Dog-patients	Post injection	1 month	3 months	+12 months
# symptom free		9/10	7/10	5/10
# significant pain reduction				2/10
# standard care (discectomy)		1/10	3/10	3/10
comment	Smooth gait, no adhesions, no incisional bulging, excellent CT im-		lasting 10. Function is still in this dog.	3/10 dogs already had advanced Pfirrmann score at the onset of the study; discectomy will follow as standard care.



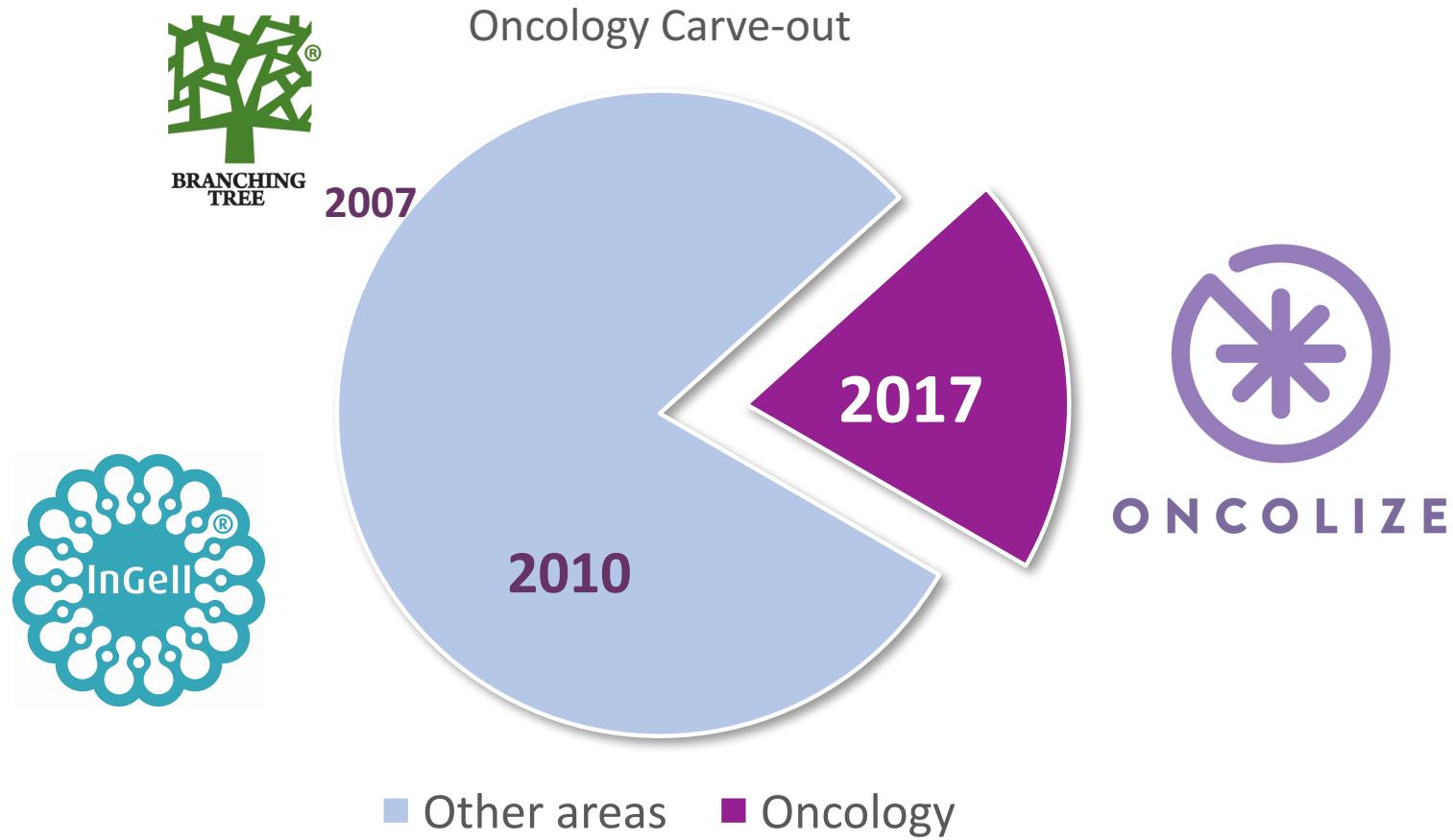
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ONCOLIZE
PRECISE CANCER MEDICINE

“we treat tumors from the inside”

InGel® technology for Oncology: OncoLize



Rare, Deadly, Solid Tumors

EU new cases /year

1. Brain Tumors	43,000
2. Pancreatic tumors	79,000
3. Untreatable prostate cancer	80,000

Unmet needs

Longer Survival

Improved Quality-of-Life

Lower Cost of Care

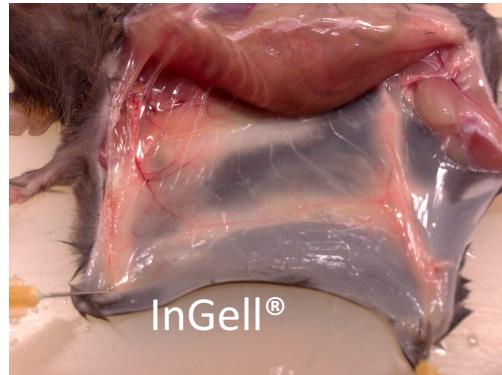
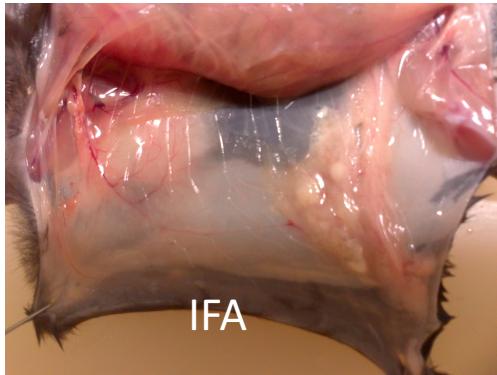
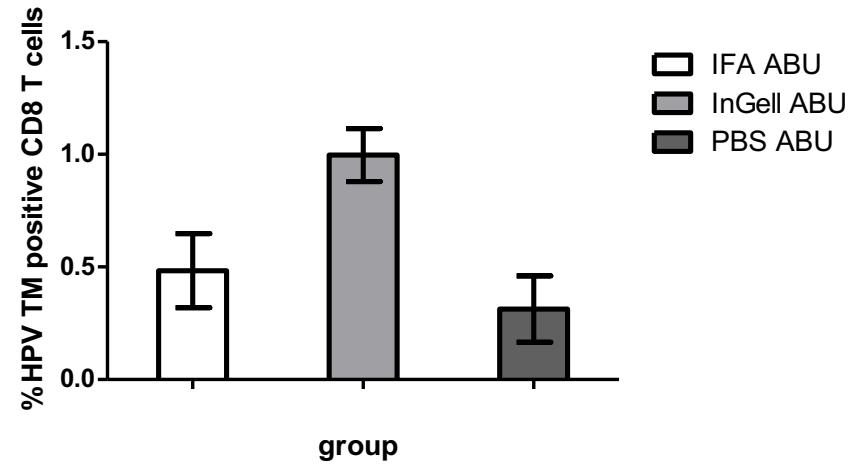
What? 'Localize it'

1. Improve drug Pharmaco-kinetics - treat it from the inside
2. Reduce burden of therapies - use less for more impact
3. Reduce costs to society

“Your solution can reduce our patient costs by €15.000 – 30.000 year”

Tumor Vaccine studies: single long peptide (4kD)

InGell; HPV RAHYNIVTF specific T cells in peripheral blood 6 days after boost vaccination, SEM, 22-07-2014



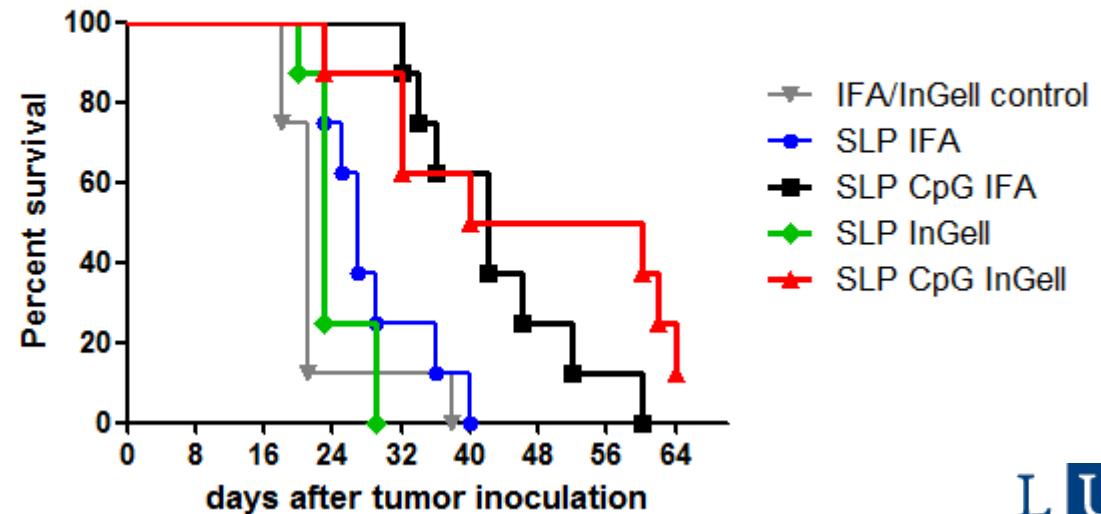
Compared to gold standard:

- Equal injectability
 - Higher titers
 - No scar formation!

Tumor Vaccine studies

preliminary studies

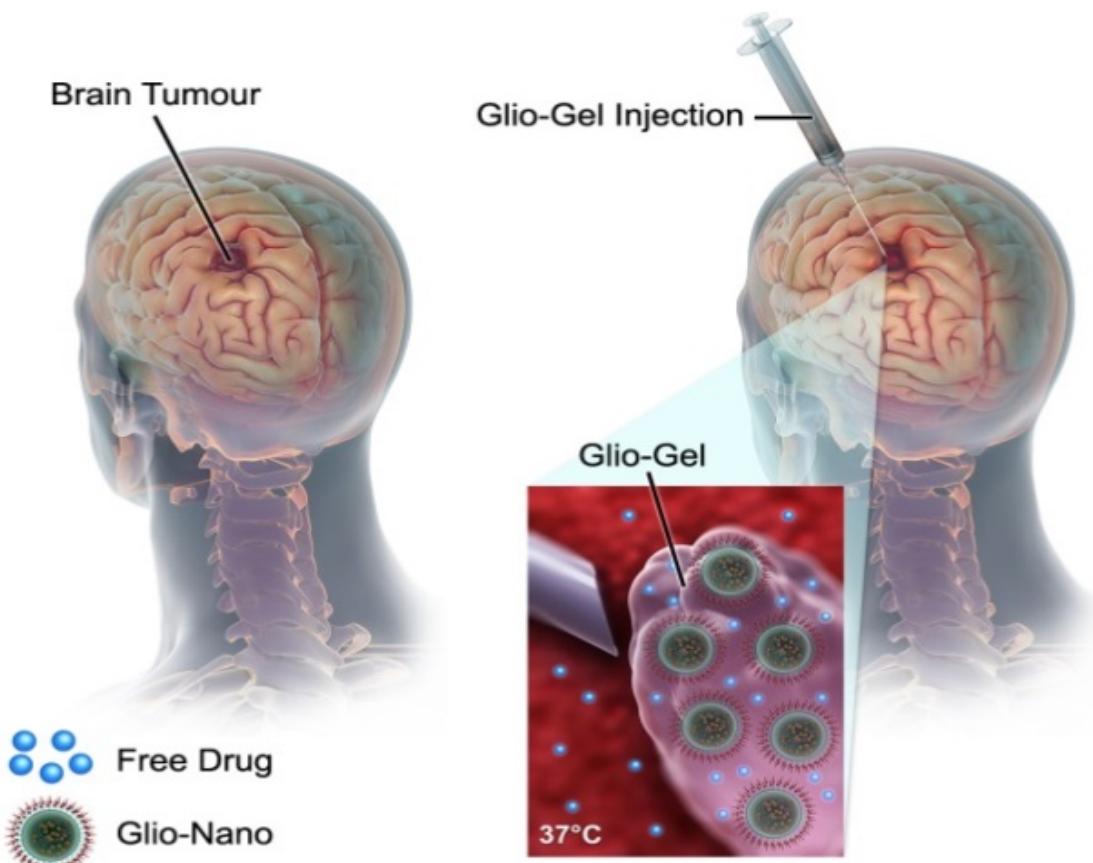
**Survival mice TC1 therapeutic treatment HPV SLP (+/- CpG) in IFA or InGell,
3Dec2014**



Leids Universitair
Medisch Centrum

- Improved survival using InGell Gamma (red line) compared to the standard Incomplete Friend's Adjuvant (black line)
- Tumor volume growth slowed down significantly within InGell arm (not shown)

GlioGel™ for Brain Tumours



Dr Eduardo Ruiz-Hernandez (RCSI)
Adv Healthc Mater. 2014 Jun;3(6):854-9

Access:

- Biopsy borehole
- Surgery borehole

Delivery:

- Stereo tactic imaging
- 26 G hamilton injectors
- Catheter-infusion

Depot:

- Gel forms
- 'in situ – in seconds'***

Actives:

- Chemo
- Radio-sensitizers
- Immuno

The GlioGel™ Consortium



OncoLize BV



Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin



Universiteit Utrecht





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