Zelflerende computers in de pathologie

Geert Litjens
Afdeling Pathologie, Radboudumc

Radboudumc

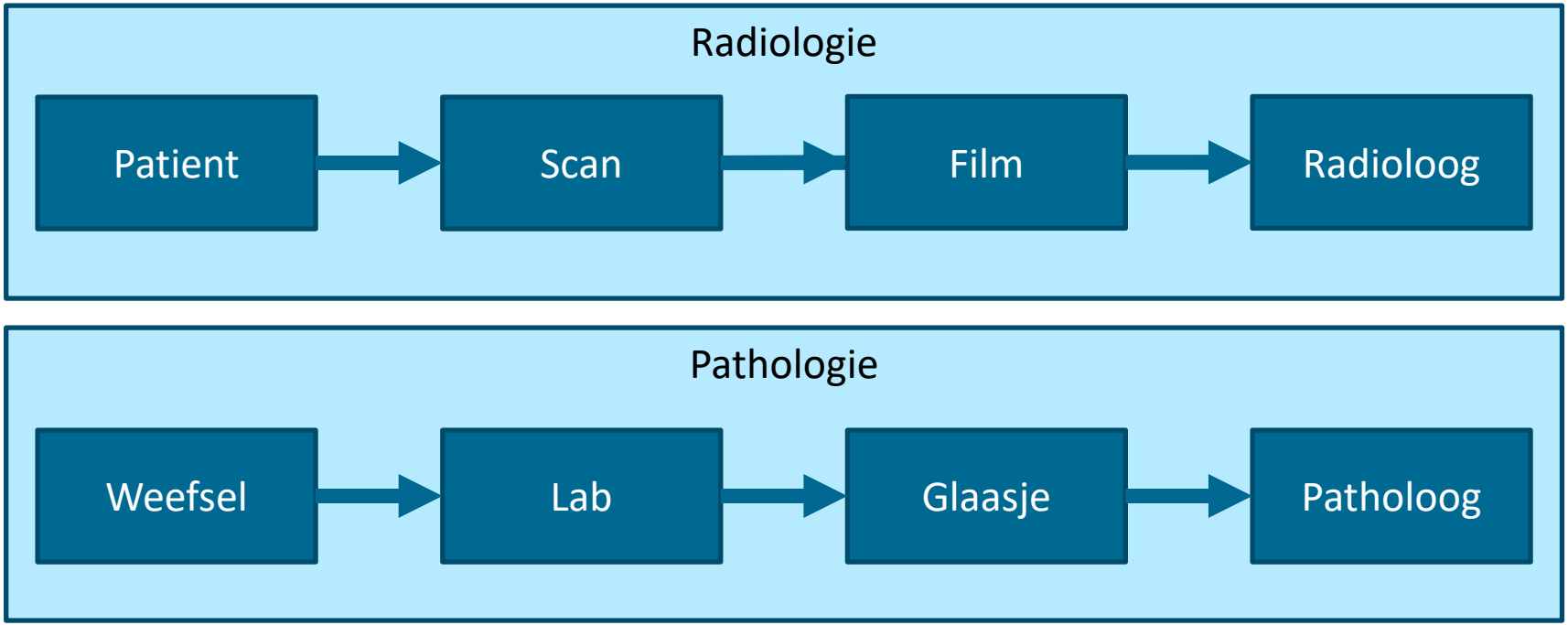
Dag van de Pathologie

Disclosure belangen spreker

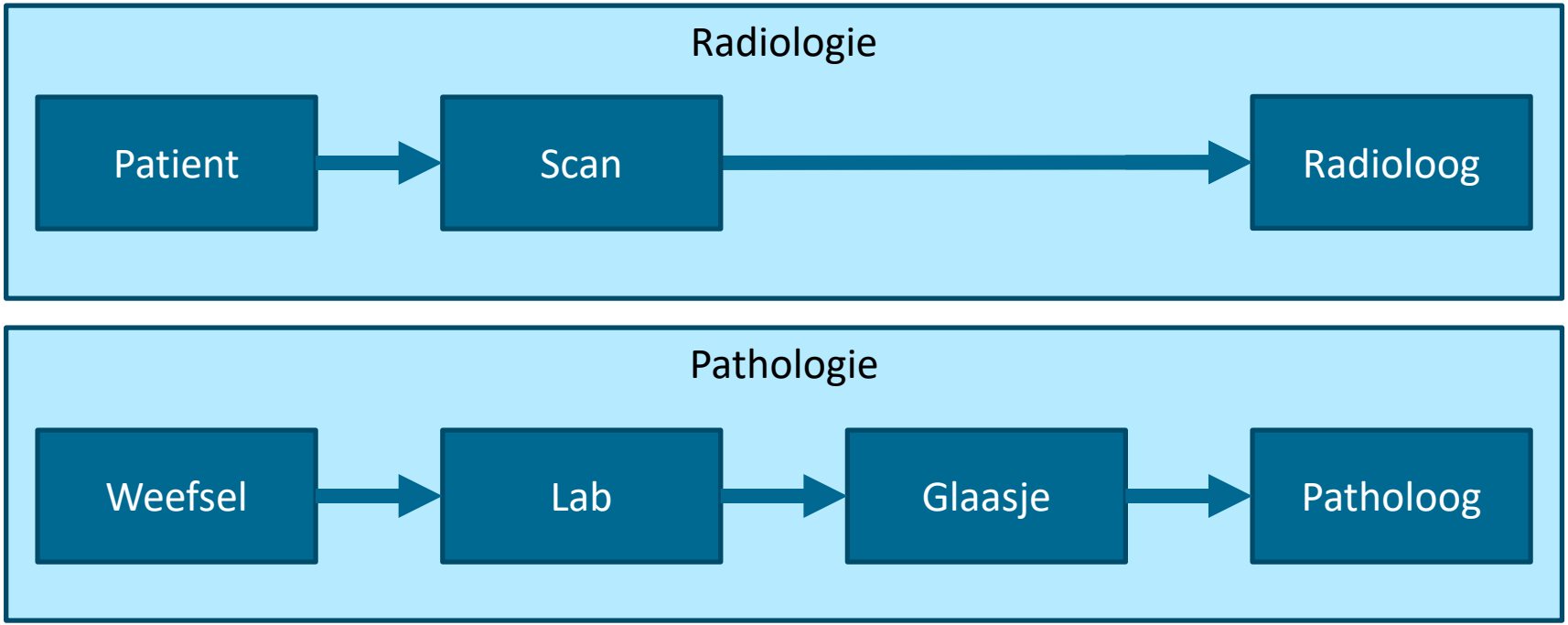
(potentiële) belangenverstrengeling	Zie hieronder
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Bedrijfsnamen
• Onderzoeksgeld	• Philips Healthcare

De belofte van de digitale pathologie?

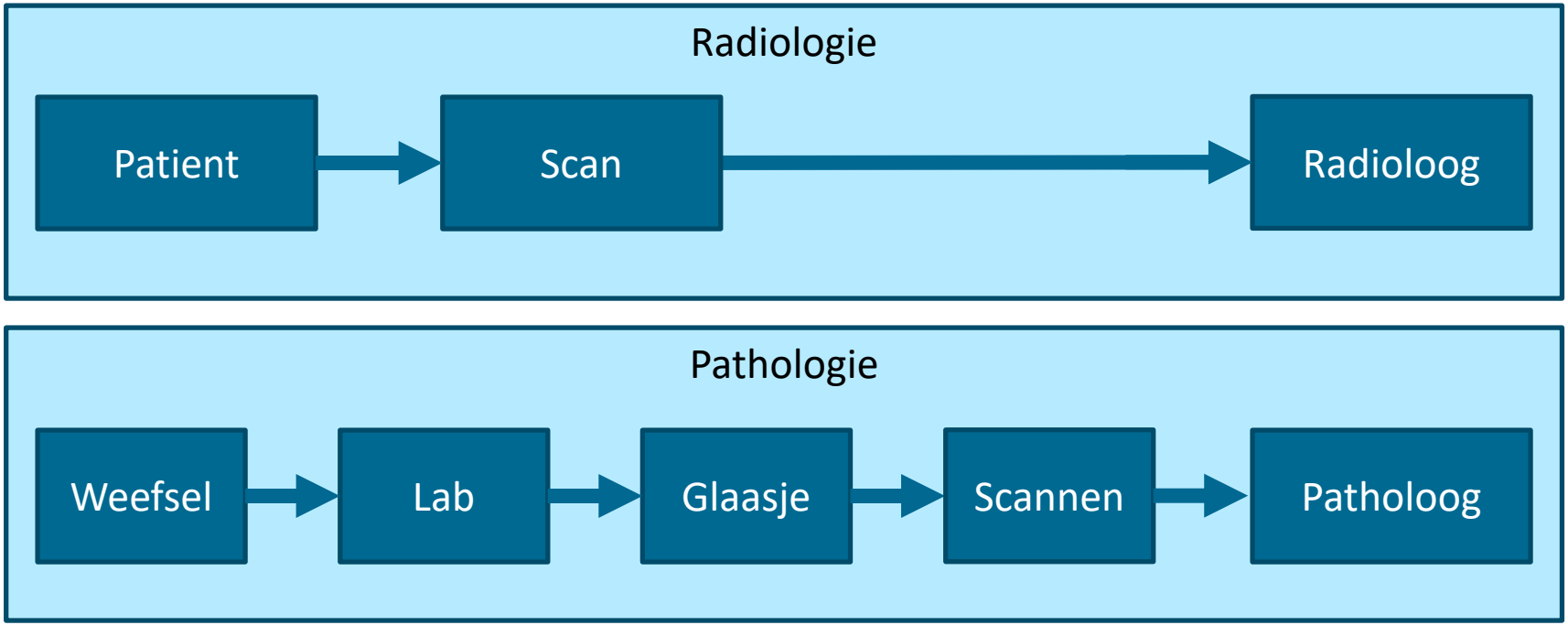
De belofte van de digitale pathologie?



De belofte van de digitale pathologie?



De belofte van de digitale pathologie?



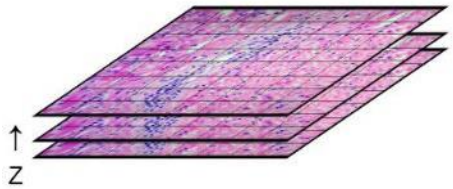
De belofte van de digitale pathologie?

Scanners

Opslag

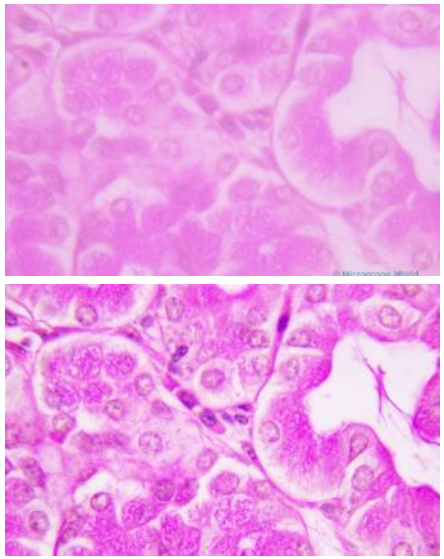
Computers

De belofte van de digitale pathologie?



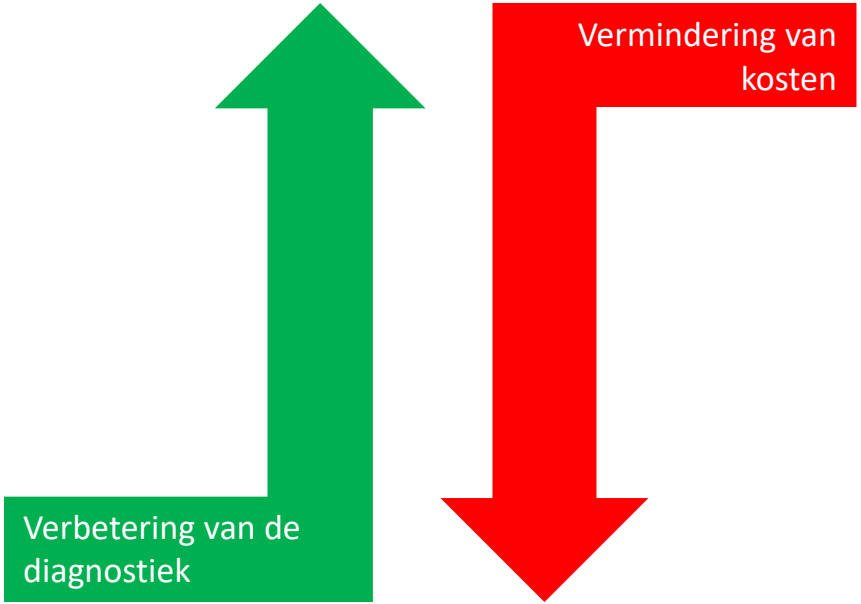
Meerdere focuspunten

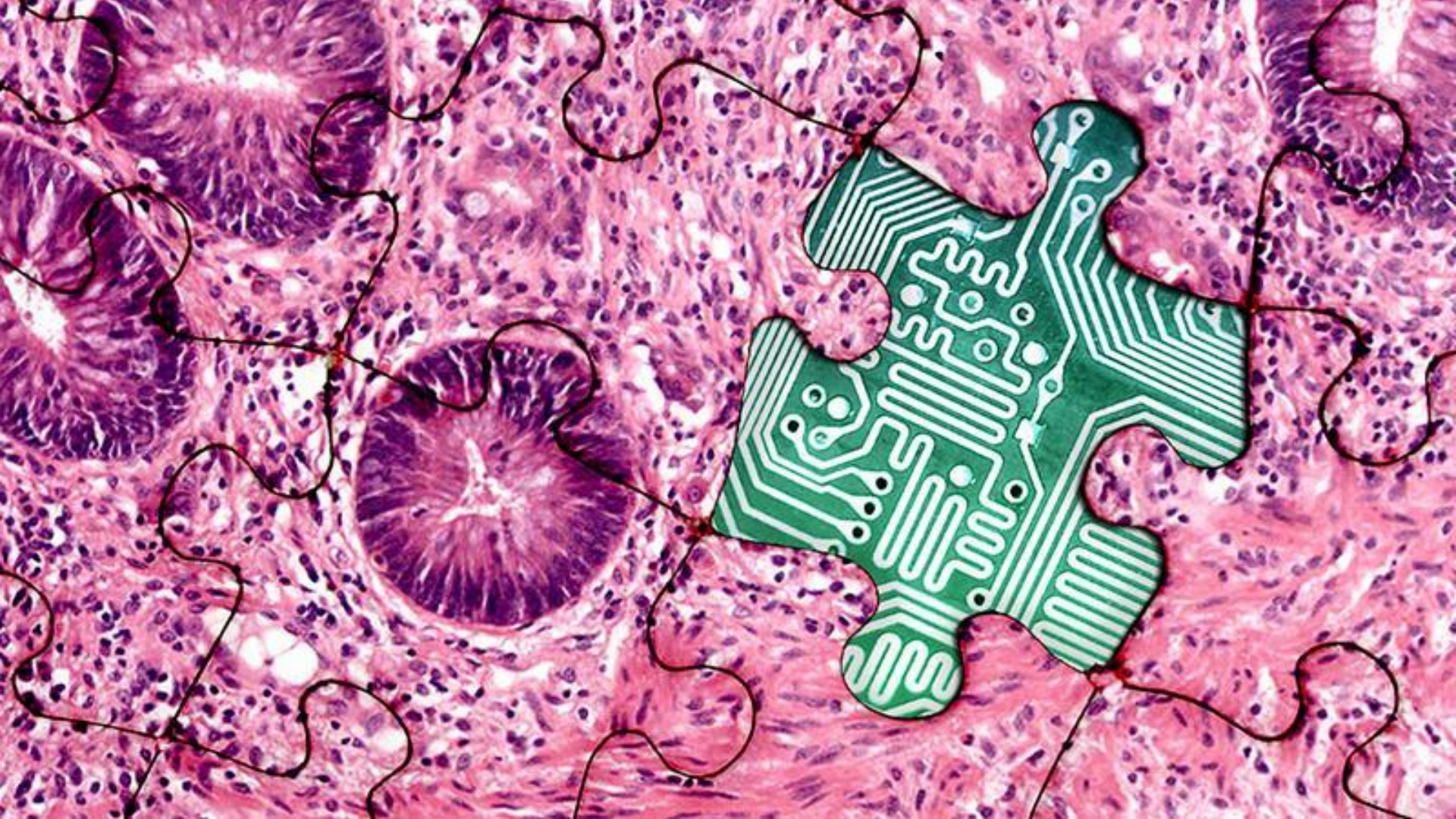
Grote objectglaasjes



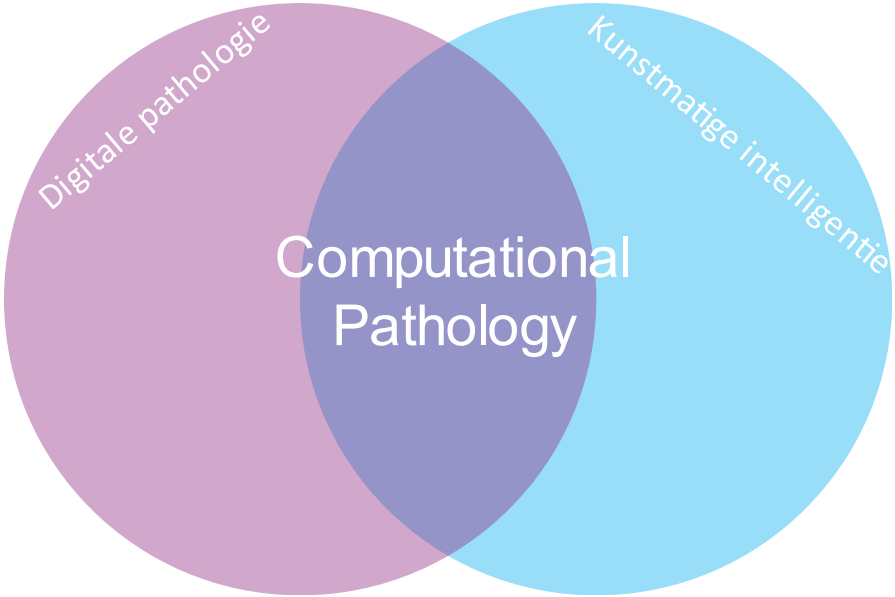
Olie-immersie

De belofte van de digitale pathologie?





Computational Pathology

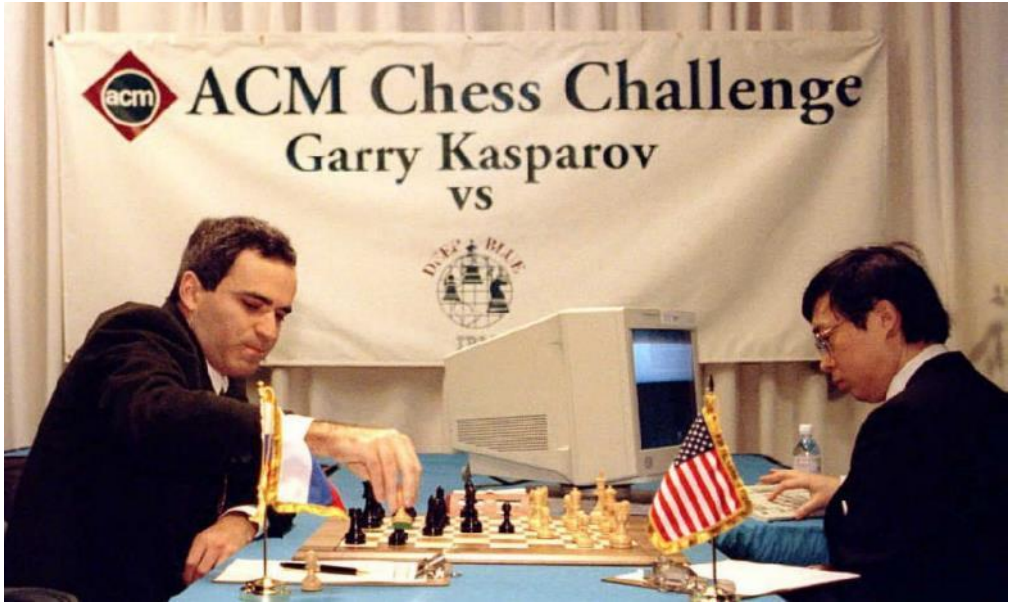


Kunstmatige intelligentie


Het Parool

Help, de robots komen eraan!

KI: een beetje geschiedenis



nature

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

At last — a computer program that can beat a champion Go player PAGE 484

ALL SYSTEMS GO

CONSERVATION

SONGBIRDS À LA CARTE

Illegal harvest of millions of Mediterranean birds

PAGE 452

RESEARCH ETHICS

SAFEGUARD TRANSPARENCY

Don't let openness backfire on individuals

PAGE 459

POPULAR SCIENCE

WHEN GENES GOT 'SELFISH'

Dawkins's calling card forty years on

PAGE 462

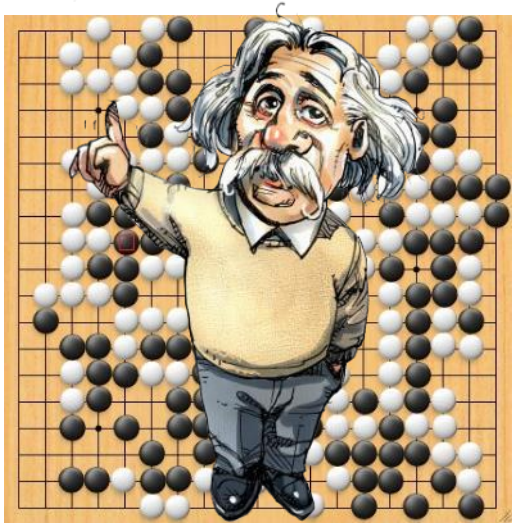
NATURE.COM/NATURE

28 January 2016 £8.0

Vol. 529, No. 7587

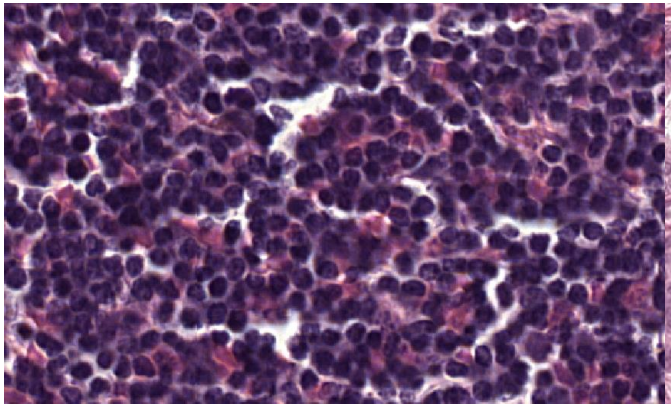
KI: een beetje geschiedenis

30 zetten gemiddeld per beur
40 beurten per spel

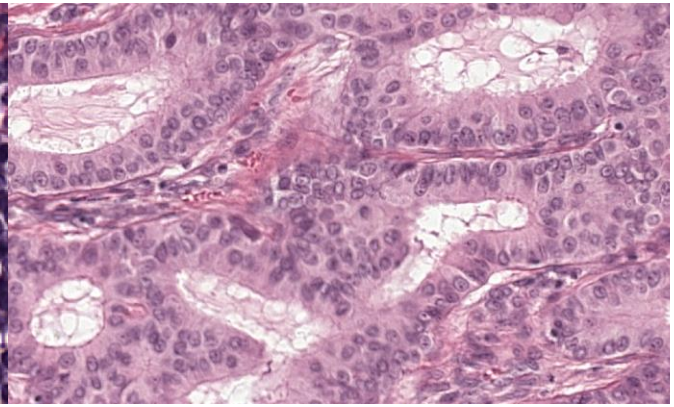


250 zetten gemiddeld per beurt
150 beurten per spel

Hoe maakte je een KI system?



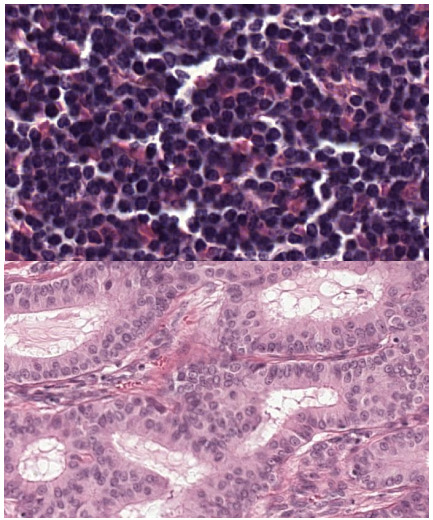
Normaal lymfeklierweefsel



Borstkankermetastase

Hoe maakte je een KI system?

Voorbeelden

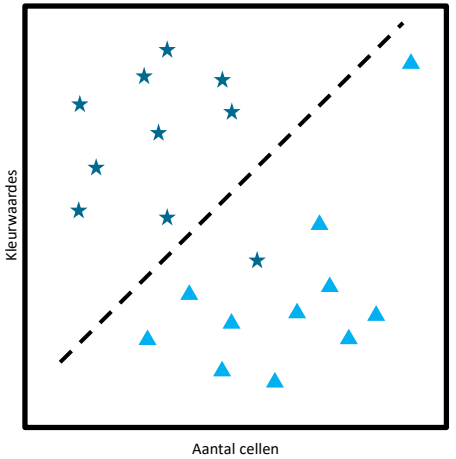


Kenmerken

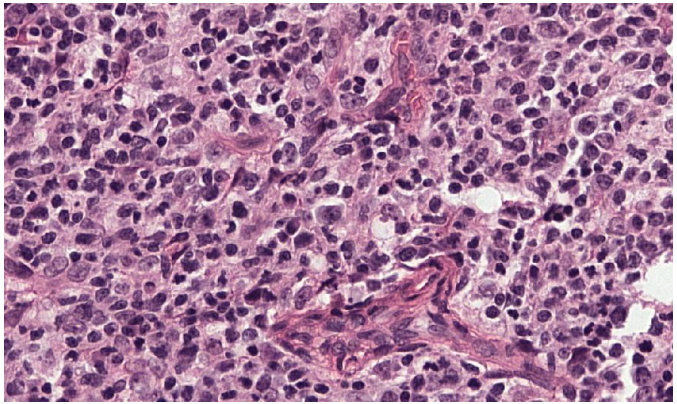
Kleurwaardes

Aantal cellen

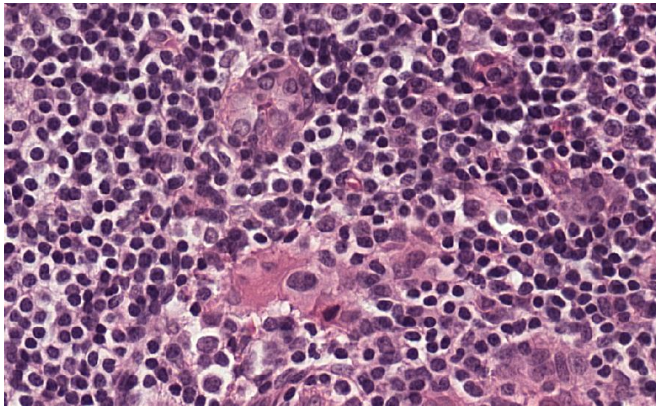
Classificeren



Hoe maakte je een KI system?



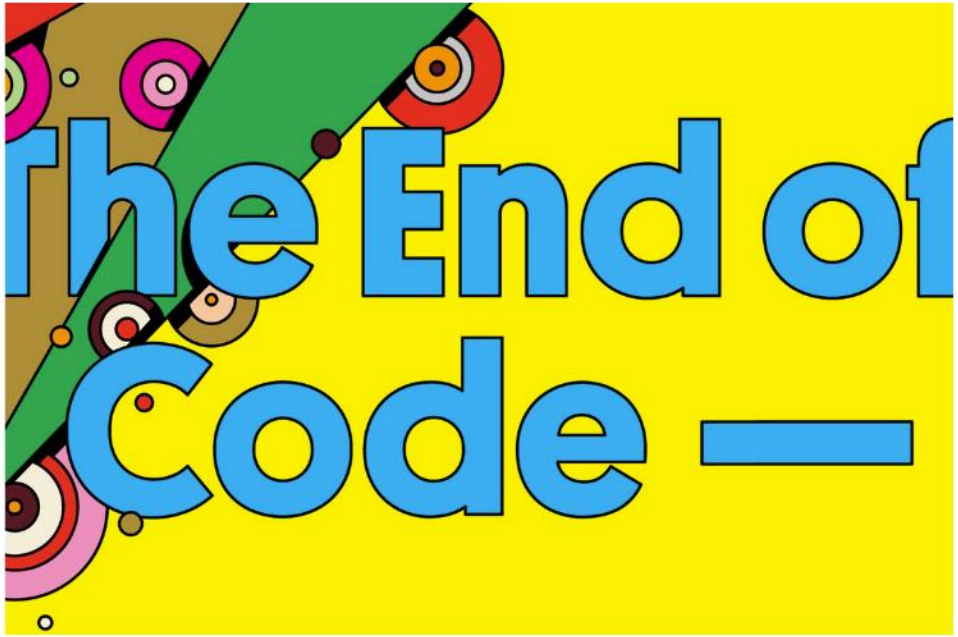
Normal lymph node



Metastasis

JASON TANZ IDEAS 05.17.16 06:50 AM

SOON WE WON'T PROGRAM COMPUTERS. WE'LL TRAIN THEM LIKE DOGS



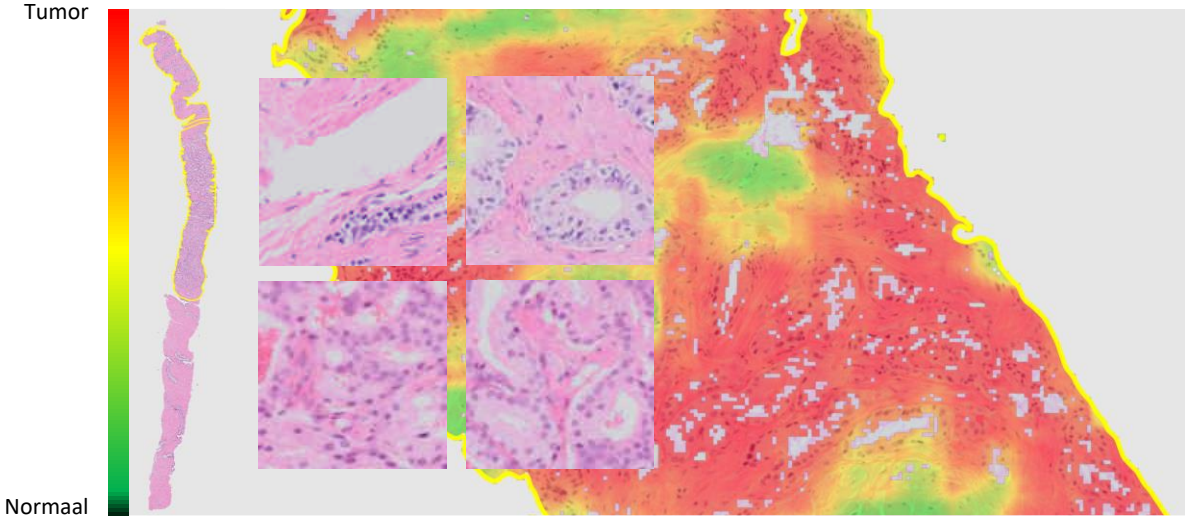
EDWARD C. MONAGHAN

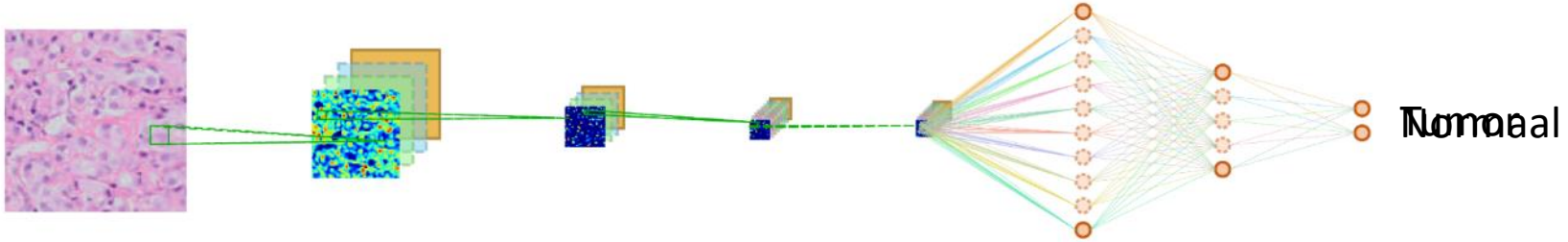
BEFORE THE INVENTION of the computer, most experimental psychologists thought the brain was an unknowable black box. You could analyze a subject's behavior—*ring bell, dog salivates*—but thoughts, memories, emotions? That stuff was obscure and inscrutable, beyond the reach of science. So these behaviorists, as they called themselves, confined their work to the study of stimulus and response, feedback and reinforcement, bells and saliva. They gave up trying to

JASON TANZ IDEAS 05.17.16 06:50 AM

SOON WE WON'T PROGRAM COMPUTERS. WE'LL TRAIN THEM LIKE DOGS

Hoe maak je nu een KI system?





Litjens et al. *Sci Rep.* 2016

Radboudumc

Zelflerende computers in de pathologie

Detectie van metastasen in lymfeklieren

Automatisch tellen van mitoses

Kwantificatie van tumor/stroma-ratio

Identificatie van tumor-geassocieerd stroma

Detectie van metastasen in lymfeklieren

H&E

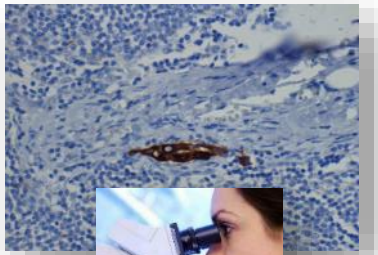
pN+

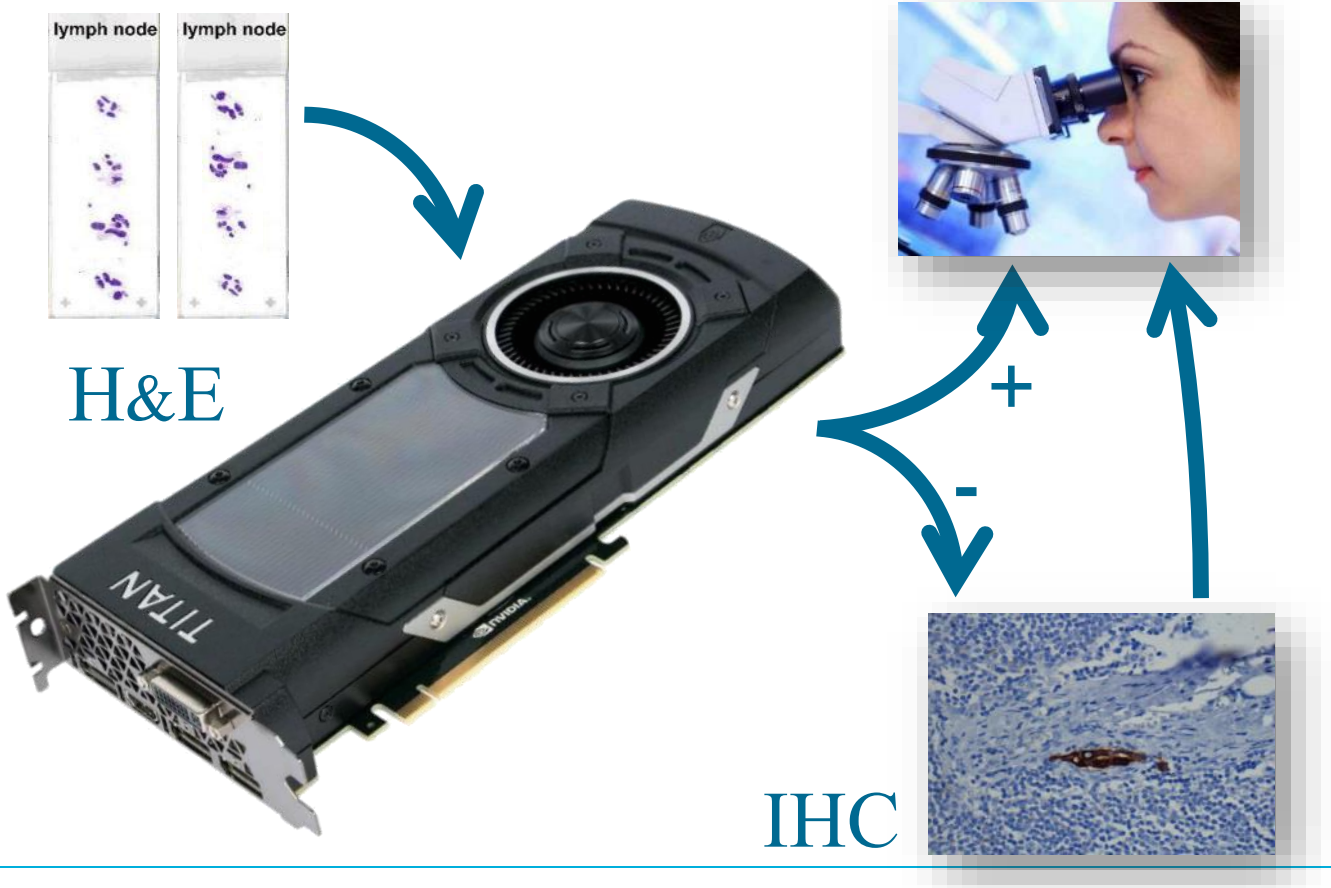
pN0

\+ + -

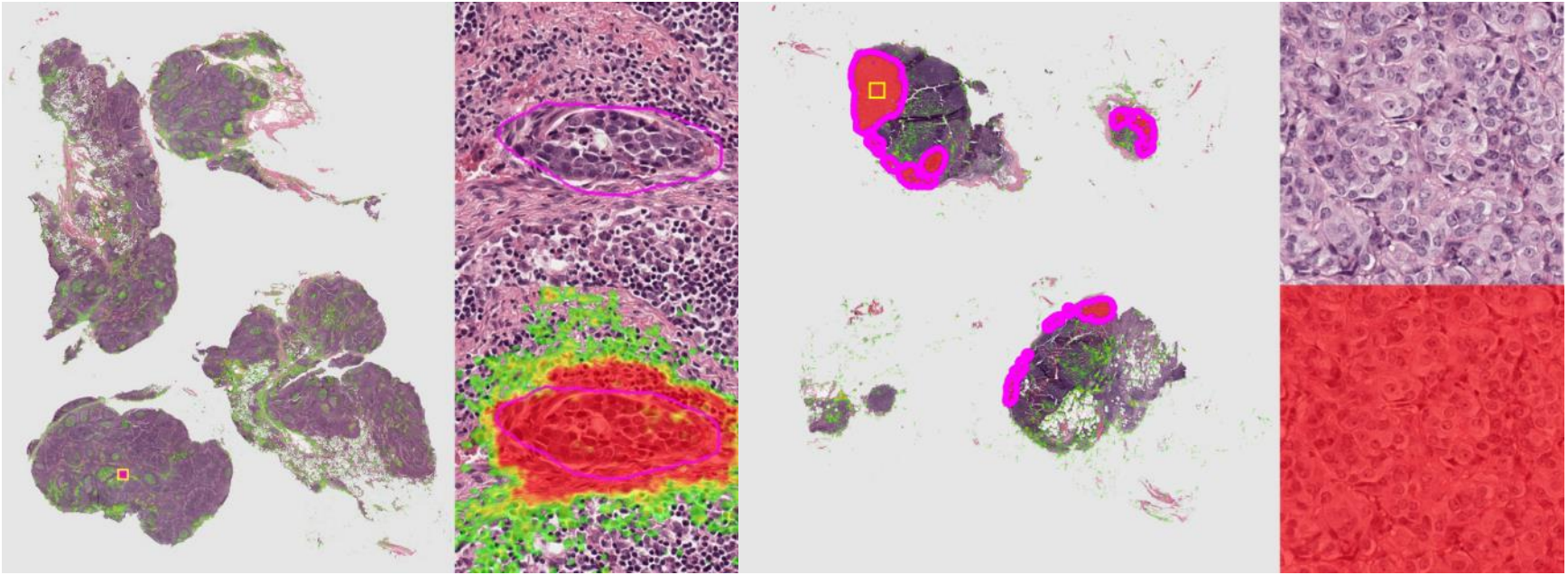
-

IHC




lymph node
lymph node
H&E
TITAN
+
-
IHC

Detectie van metastasen in lymfeklieren



Data

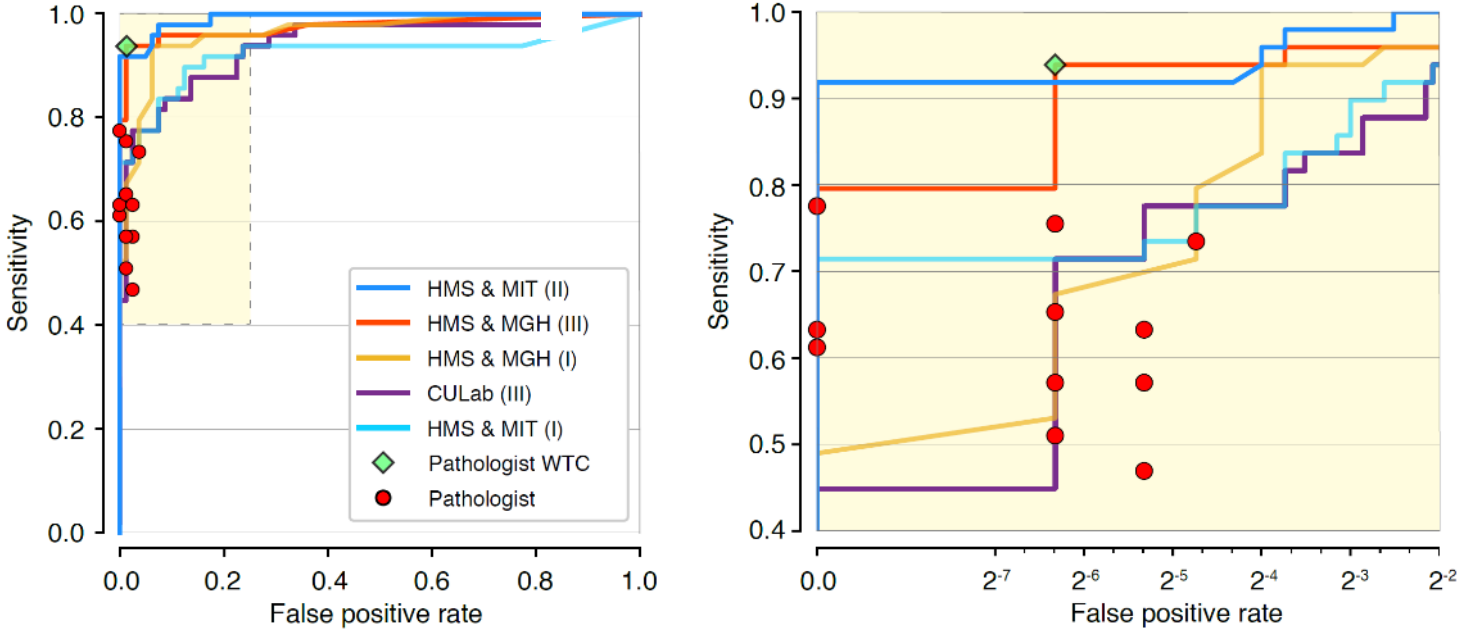
Centrum	Aantal coupes
CWZ (Nijmegen)	200
LabPON (Hengelo)	200
Rijnstate (Arnhem)	200
Radboudumc (Nijmegen)	439
UMCU (Utrecht)	350
Totaal	**1399**


CAMELYON16

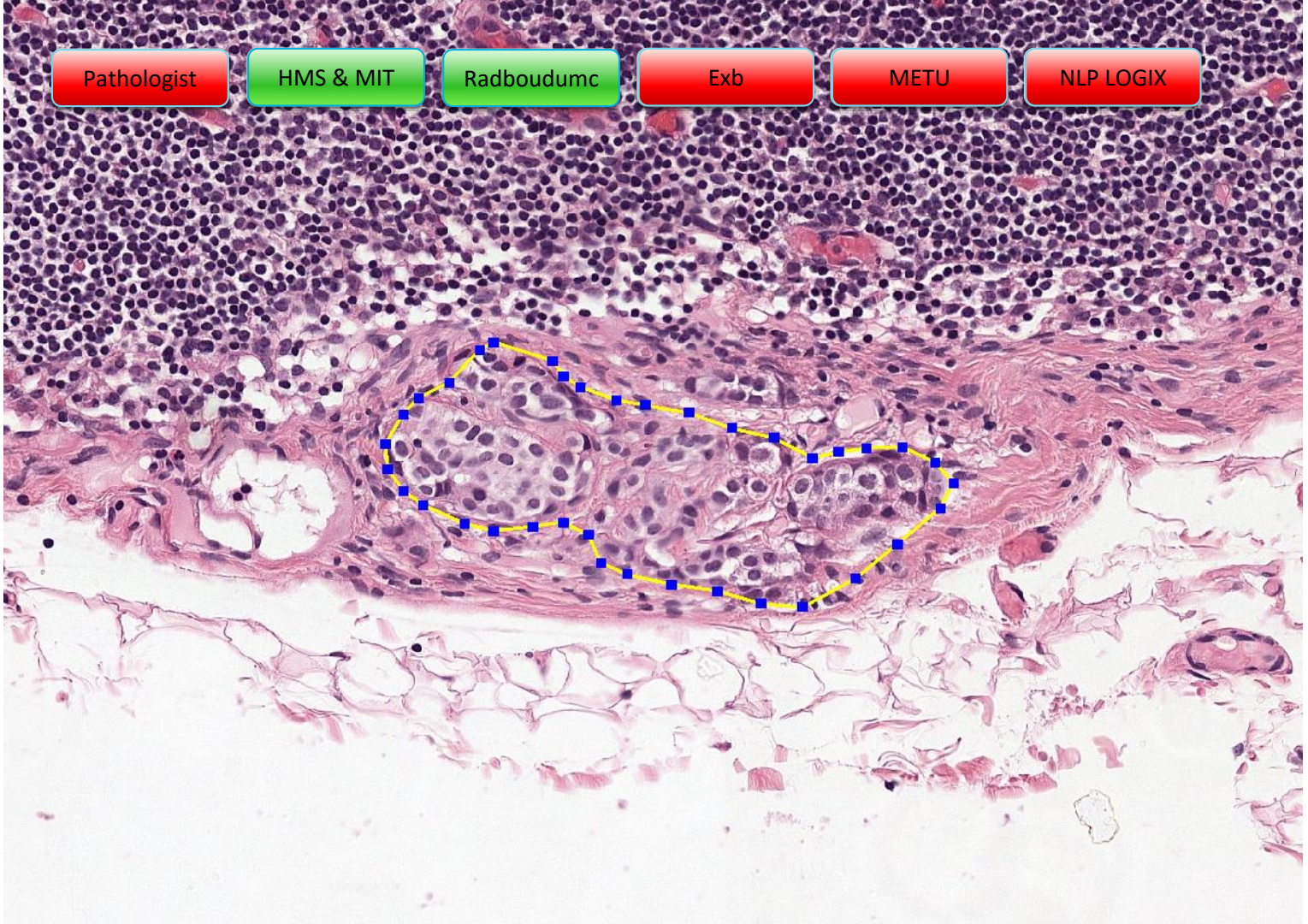

CAMELYON17

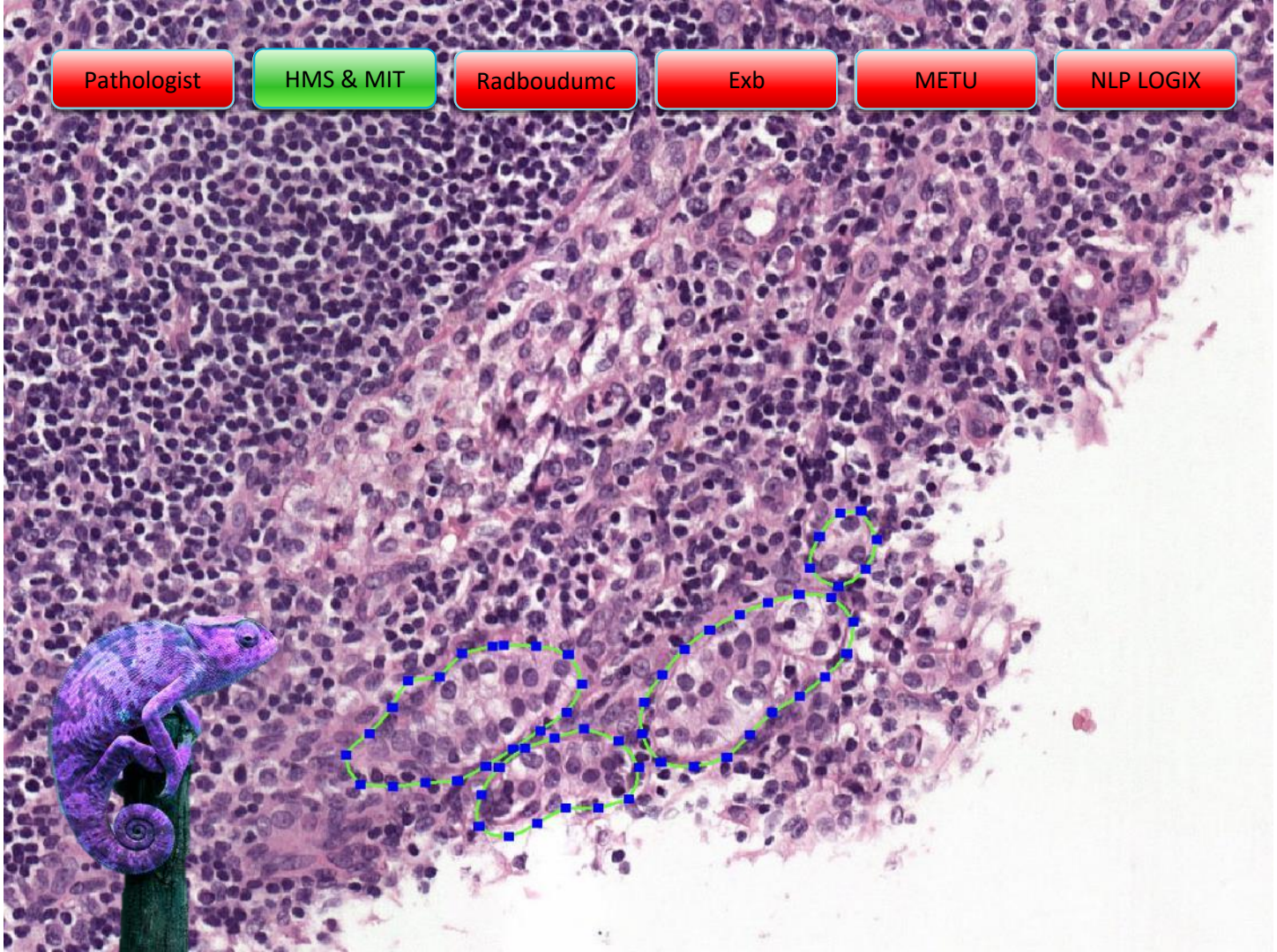
Rank	Team	AUC	Description
01	**Harvard Medical School (BIDMC) and Massachusetts Institute of Technology (CSAIL), USA**	0.9250	
02	ExB Research and Development co., Germany	0.9173	
03	Independent participant, Germany	0.8680	
04	Health Sciences Middle East Technical University, Turkey	0.8669	
05	NLP LOGIX co., USA	0.8332	
06	University of Toronto, Electrical and Computer Engineering, Canada	0.8181	
07	The Warwick-QU Team, United Kingdom	0.7999	
08	Radboud University Medical Center, Diagnostic Image Analysis Group, Netherlands	0.7828	
09	HTW-BERLIN, Germany	0.7717	
10	University of Toronto, Electrical and Computer Engineering, Canada	0.7666	

Vergelijking met de patholoog



Ehteshami et al. *JAMA. 2017*


Pathologist
HMS & MIT
Radboudumc
Exb
METU
NLP LOGIX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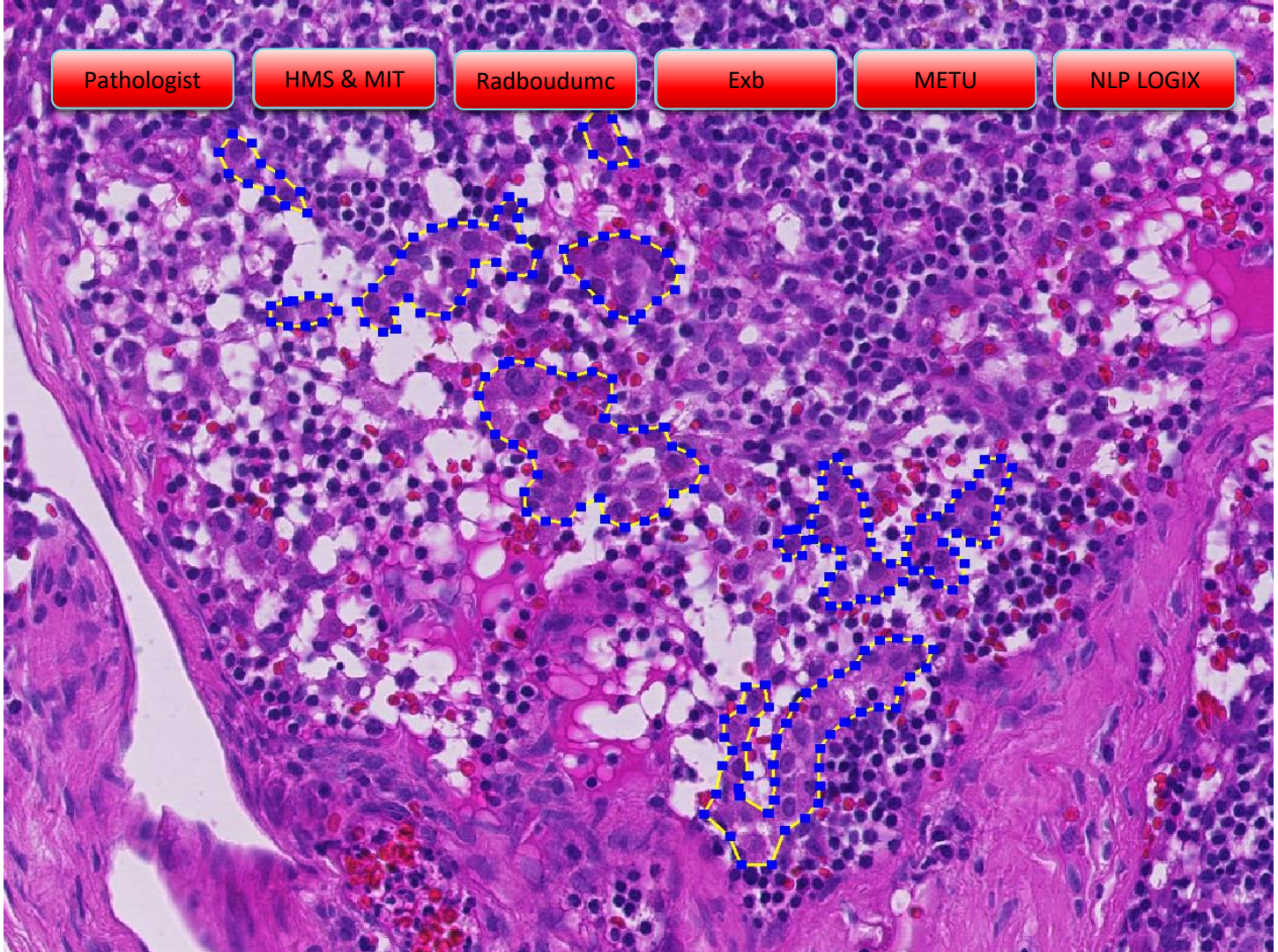
Pathologist
HMS & MIT
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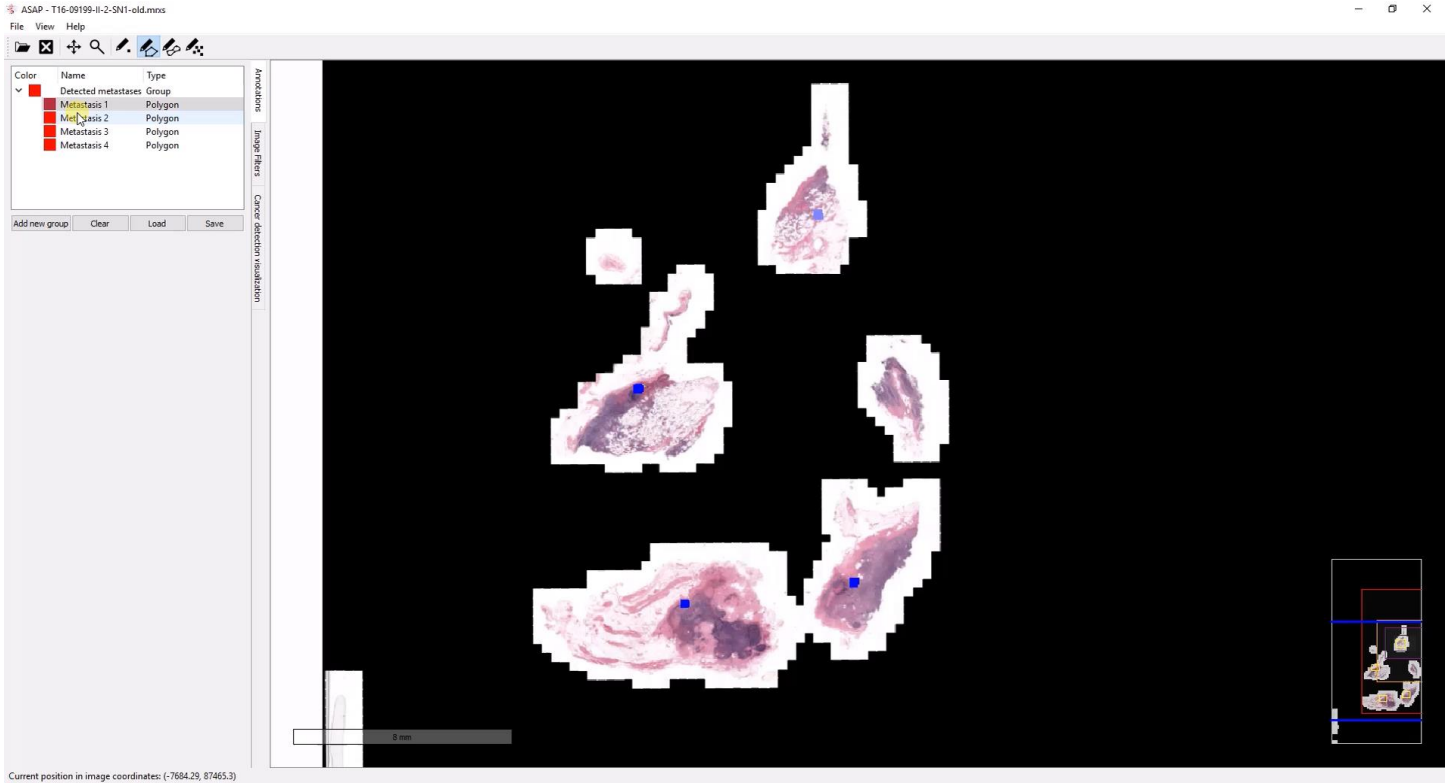
ASAP - T16-09199-II-2-SN1-old.mrxs
File
View
Help
Color
Name
Type
Detected metastases
Group
Metastasis 1
Polygon
Metastasis 2
Polygon
Metastasis 3
Polygon
Metastasis 4
Polygon
Add new group
Clear
Load
Save
Annotations
Image Filters
Cancer detection visualization
8 mm
Current position in image coordinates: (-7684.29, 87465.3)

Zelflerende computers in de pathologie

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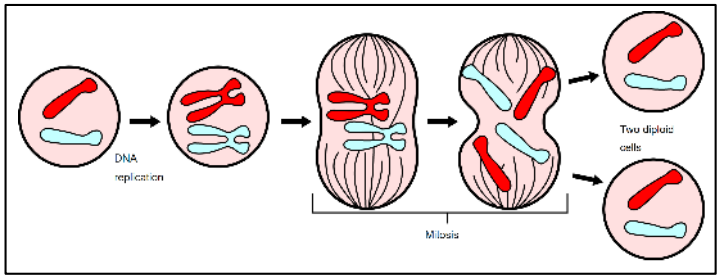
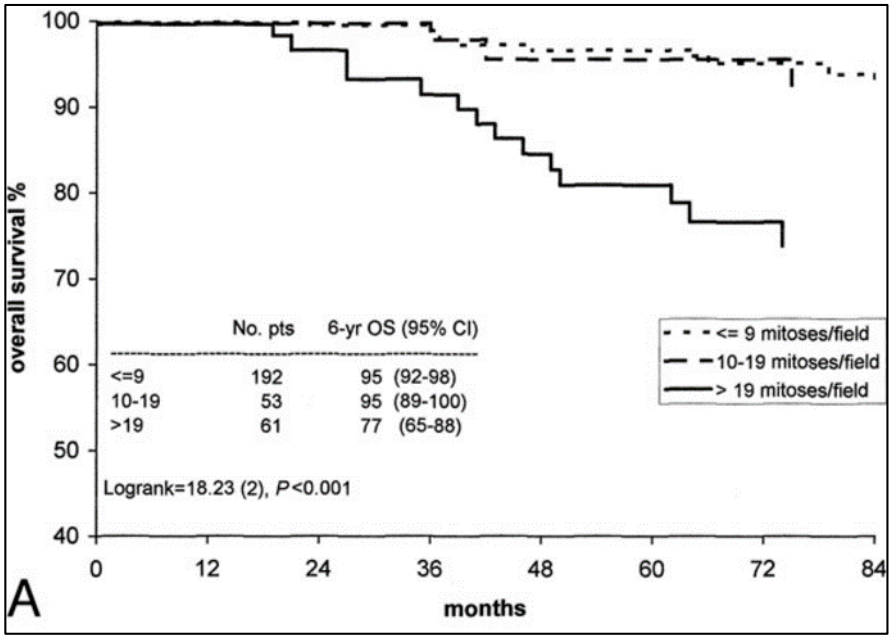
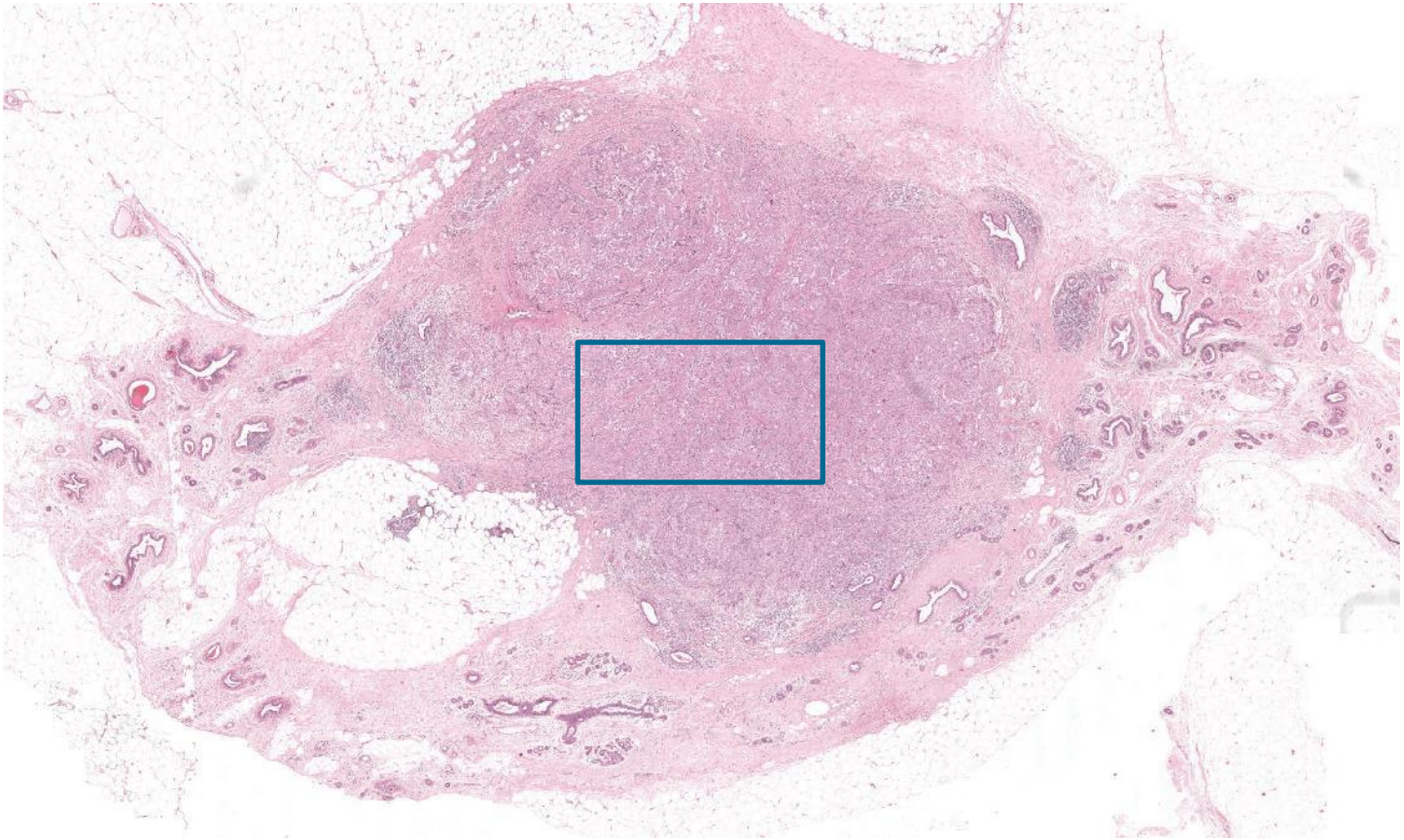
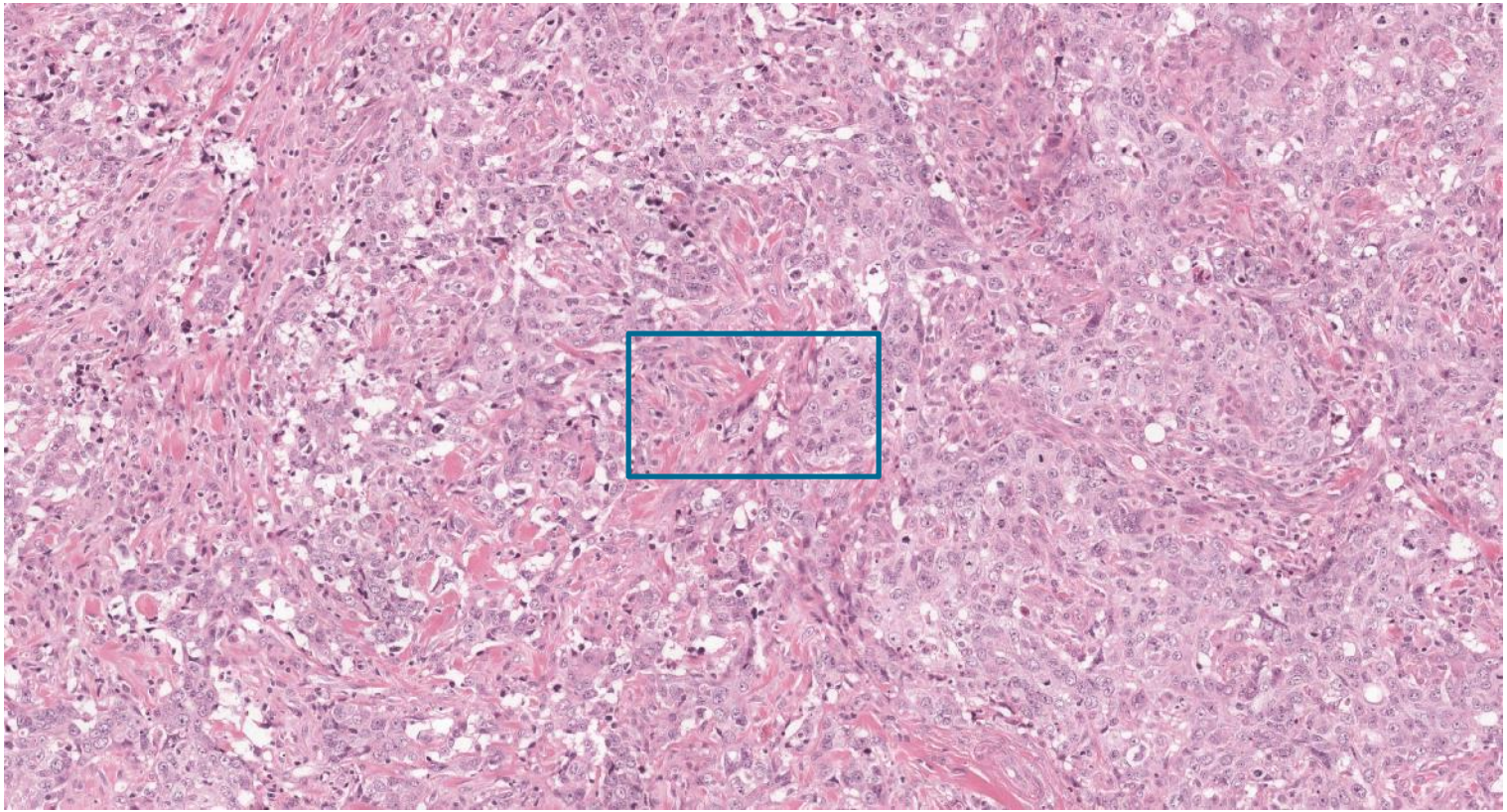
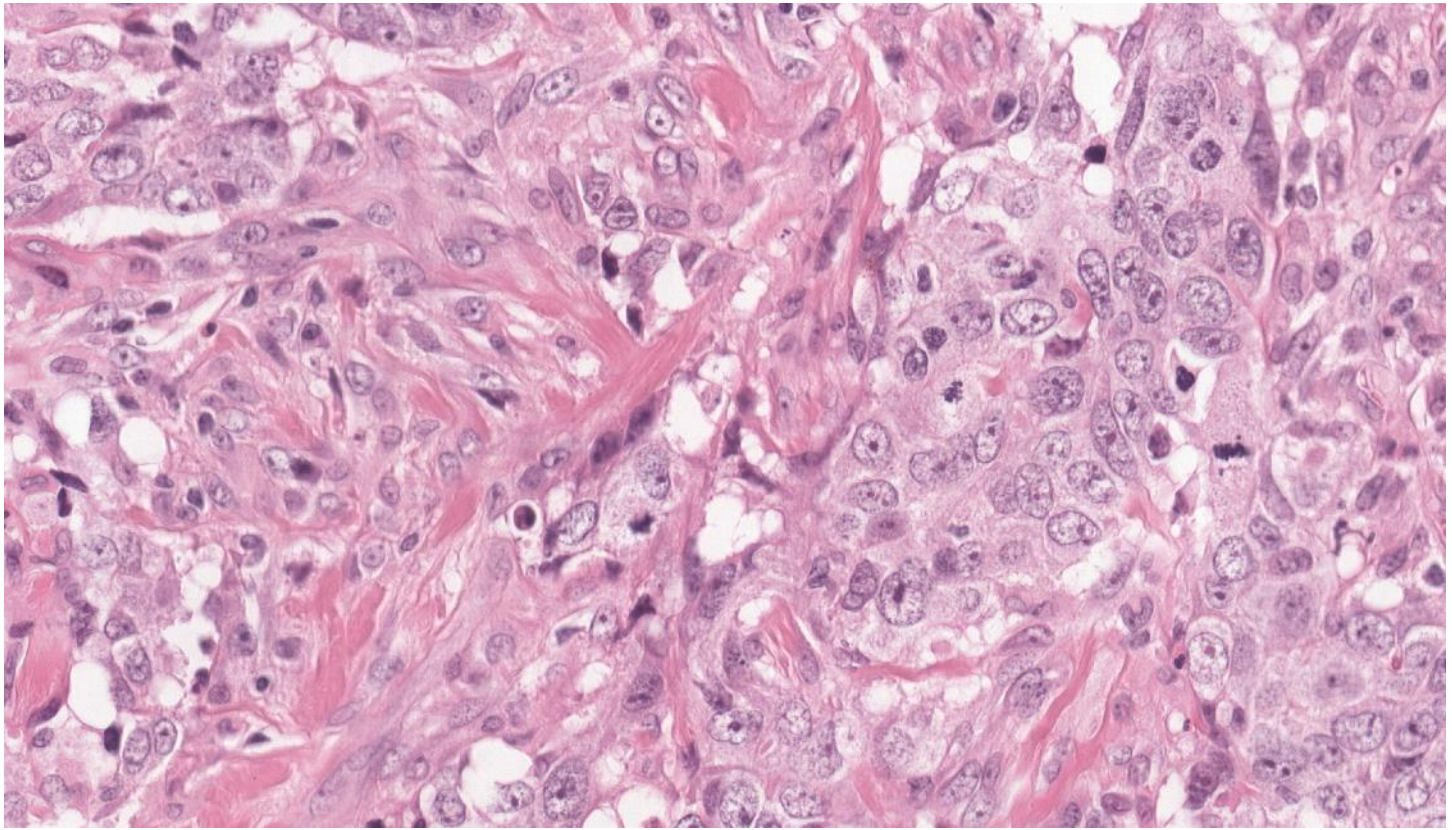






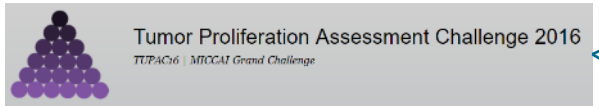




Automatisch tellen van mitoses

D. C. Cireşan, A. Giusti, L. M. Gambardella, and J. Schmidhuber, "Mitosis detection in breast cancer histology images with deep neural networks," in *International Conference on Medical Image Computing and Computer-assisted Intervention*. Springer, 2013, pp. 411–418.

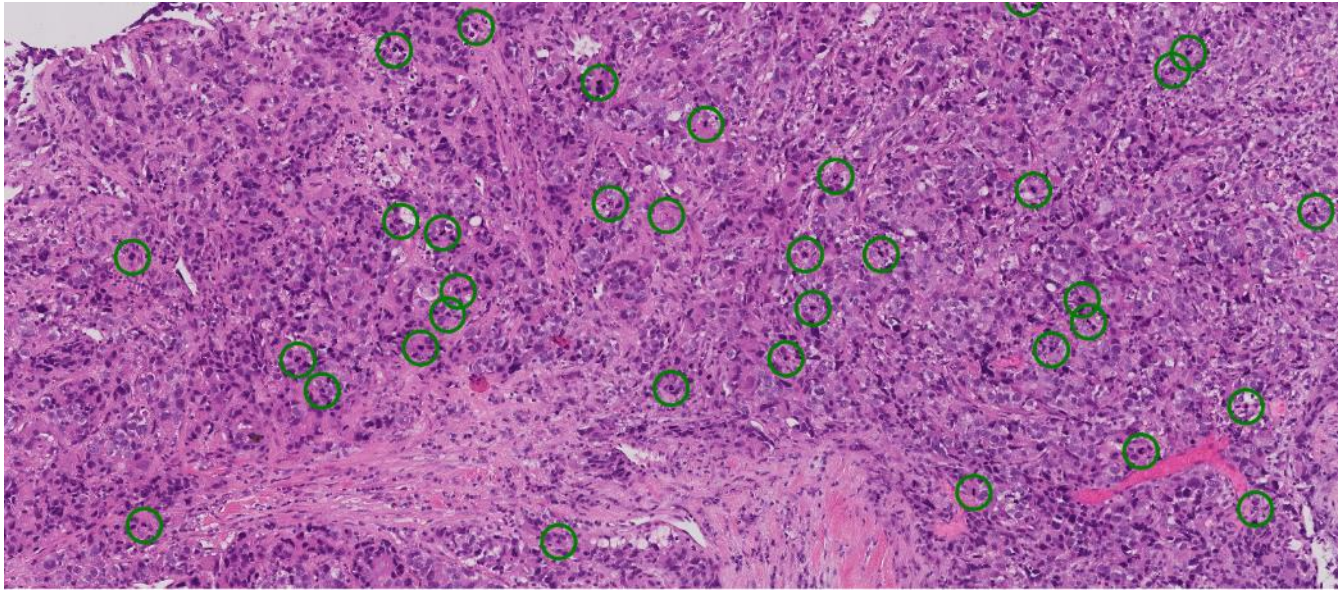
M. Veta, P. J. van Diest, M. Jiwa, S. Al-Janabi, and J. P. Pluim, "Mitosis counting in breast cancer: Object-level interobserver agreement and comparison to an automatic method," *PloS one*, vol. 11, no. 8, p. e0161286, 2016.



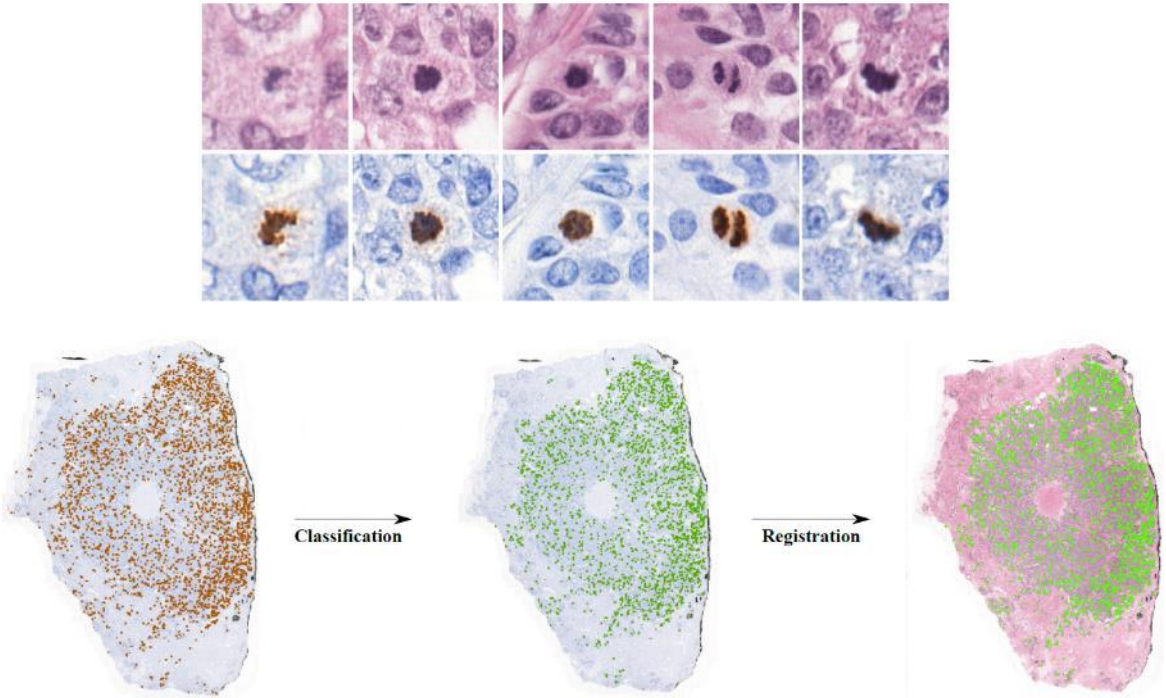
E. Zerhouni, D. Lányi, M. Viana, and M. Gabrani, "Wide residual networks for mitosis detection," in *Biomedical Imaging (ISBI 2017), 2017 IEEE 14th International Symposium on*. IEEE, 2017, pp. 924–928.

K. Paeng, S. Hwang, S. Park, M. Kim, and S. Kim, "A unified framework for tumor proliferation score prediction in breast histopathology," *arXiv preprint arXiv:1612.07180*, 2016.

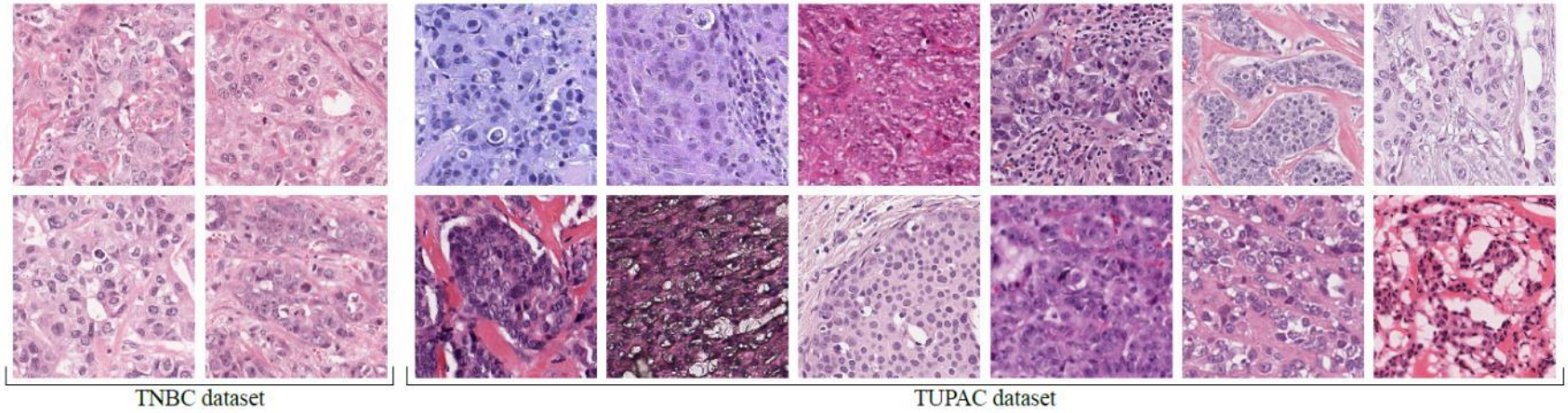
Probleem 1: referentie standaard



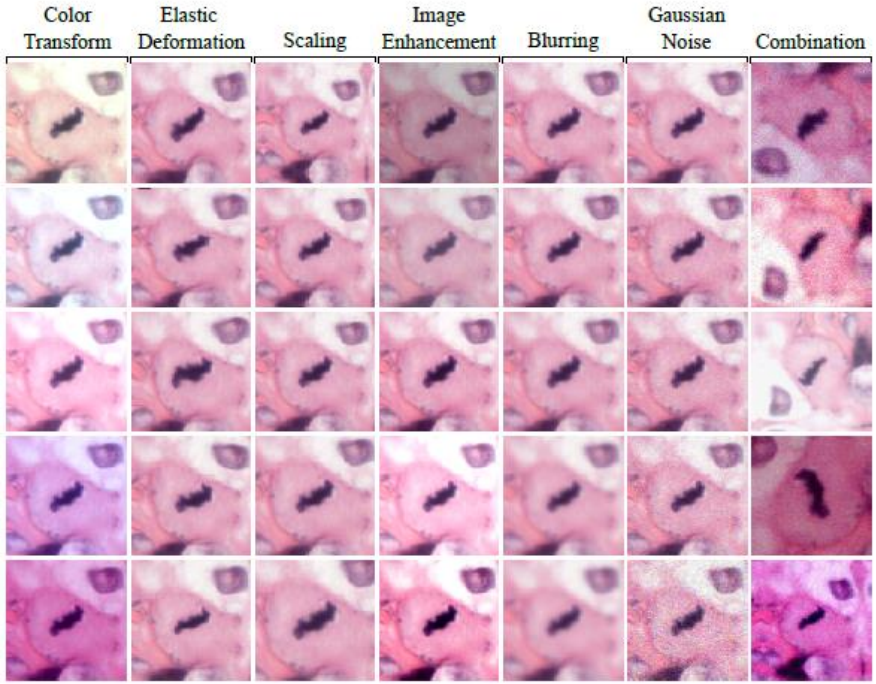
Oplossing: PHH3 IHC

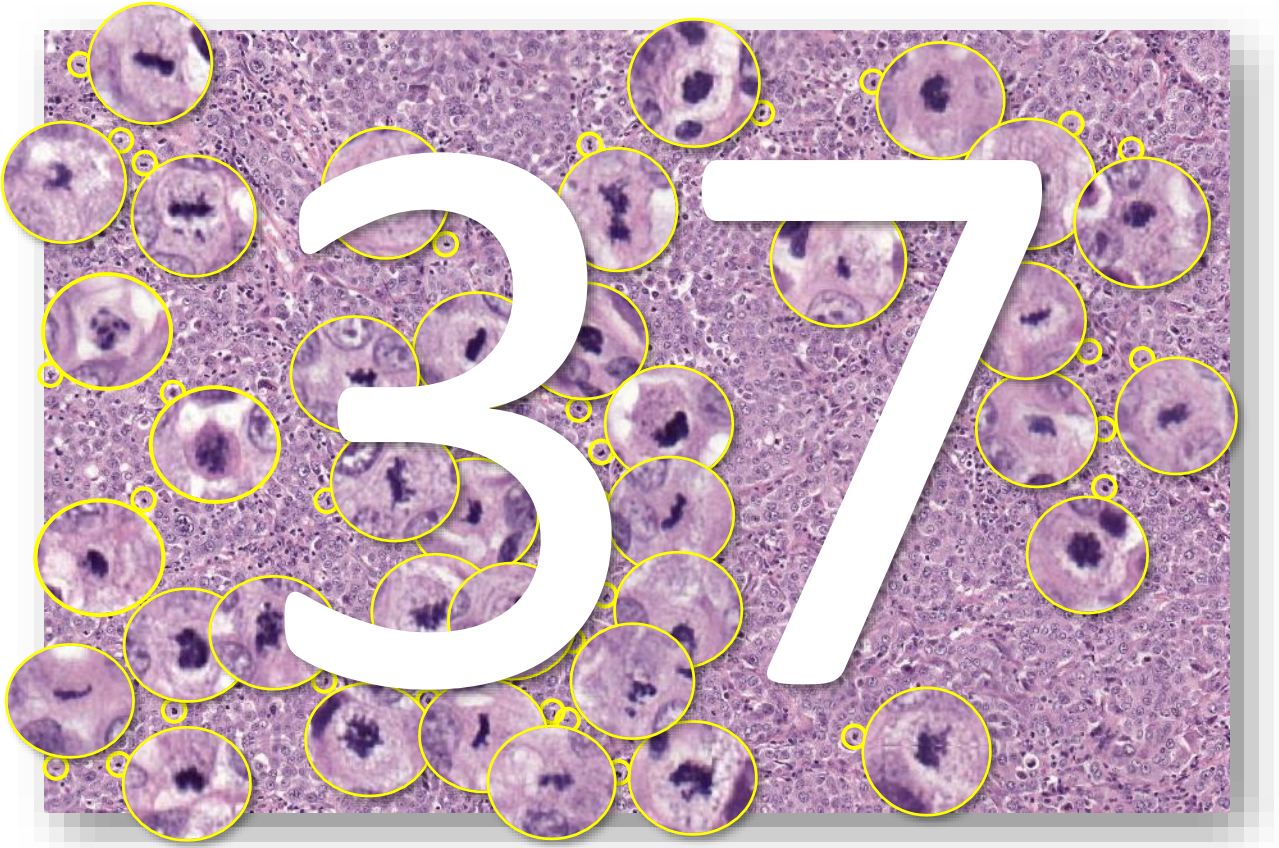


Probleem 2: kleuringsverschillen



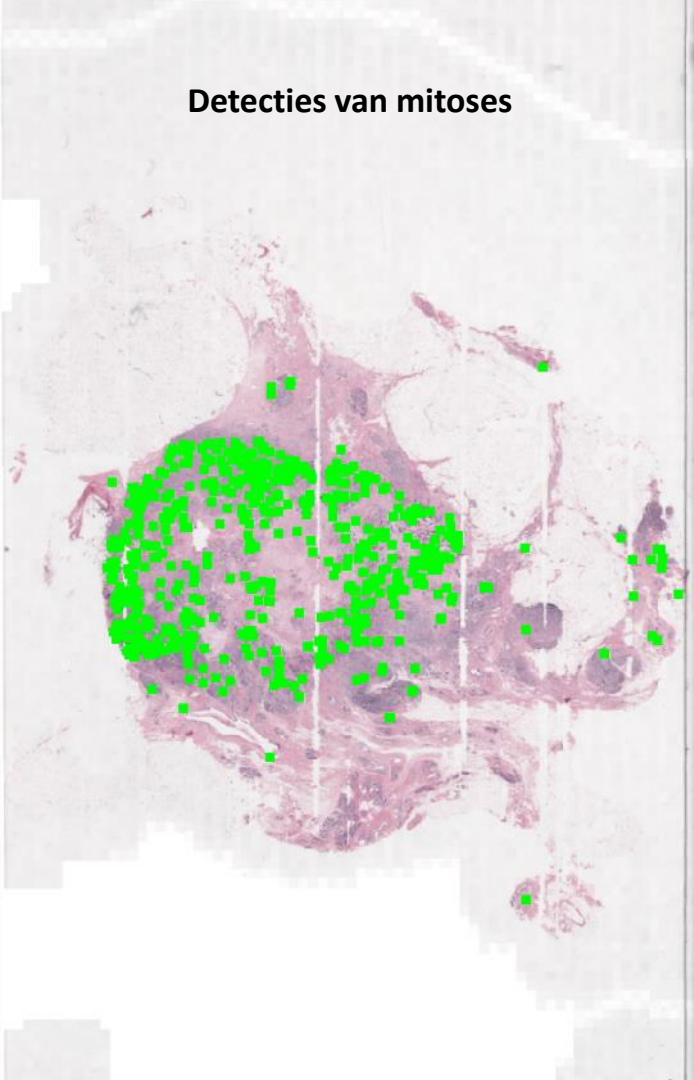
Oplossing 2: KI laten wennen aan kleurverschil



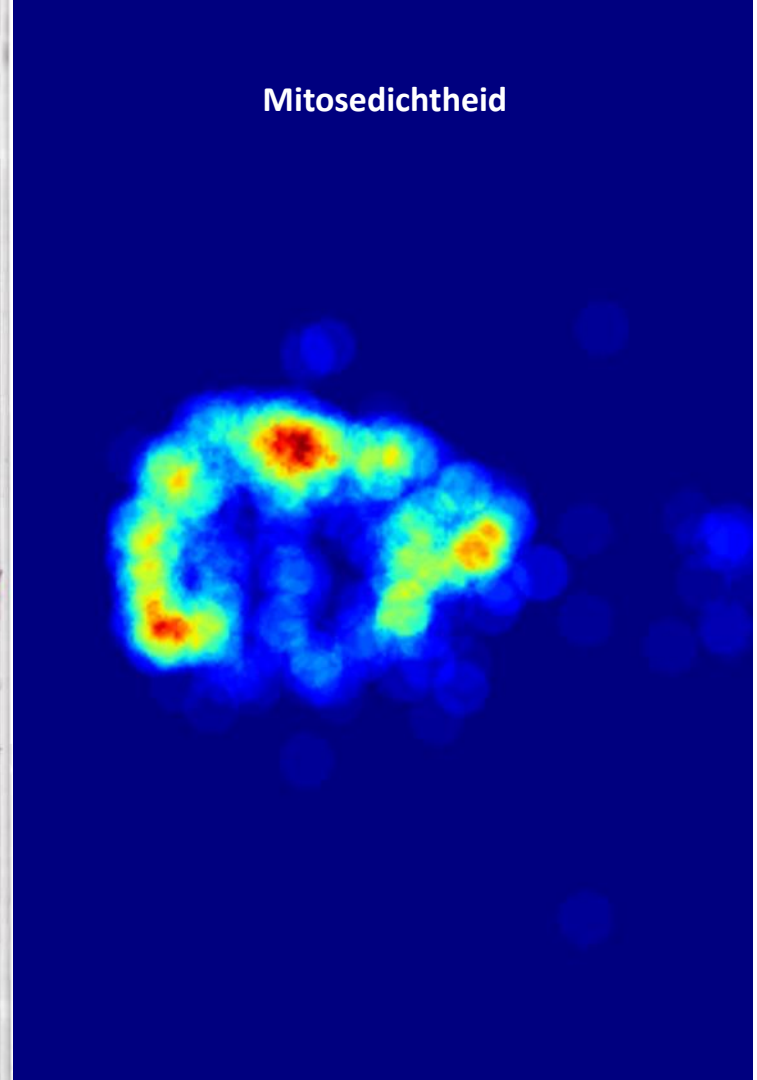


Tellez et al. *IEEE Transactions on Medical Imaging*. Accepted

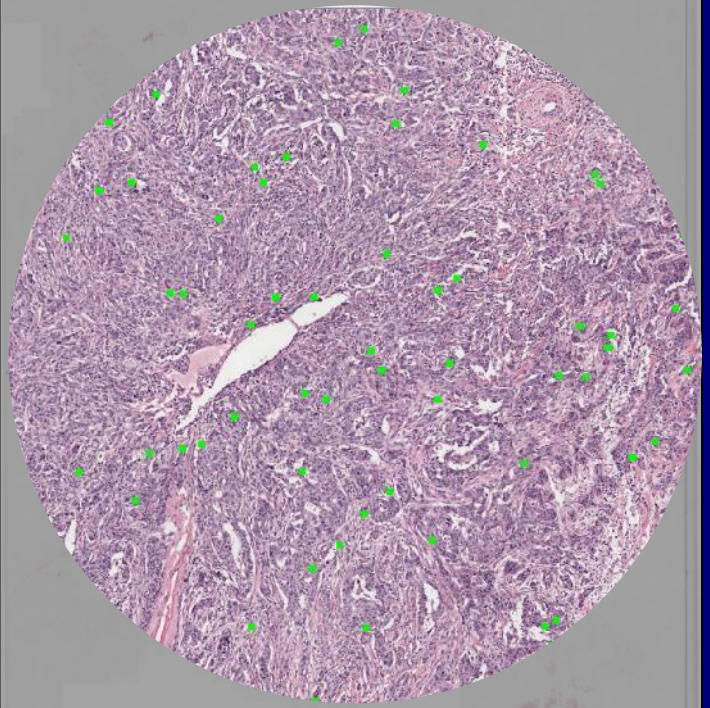
Detecties van mitoses



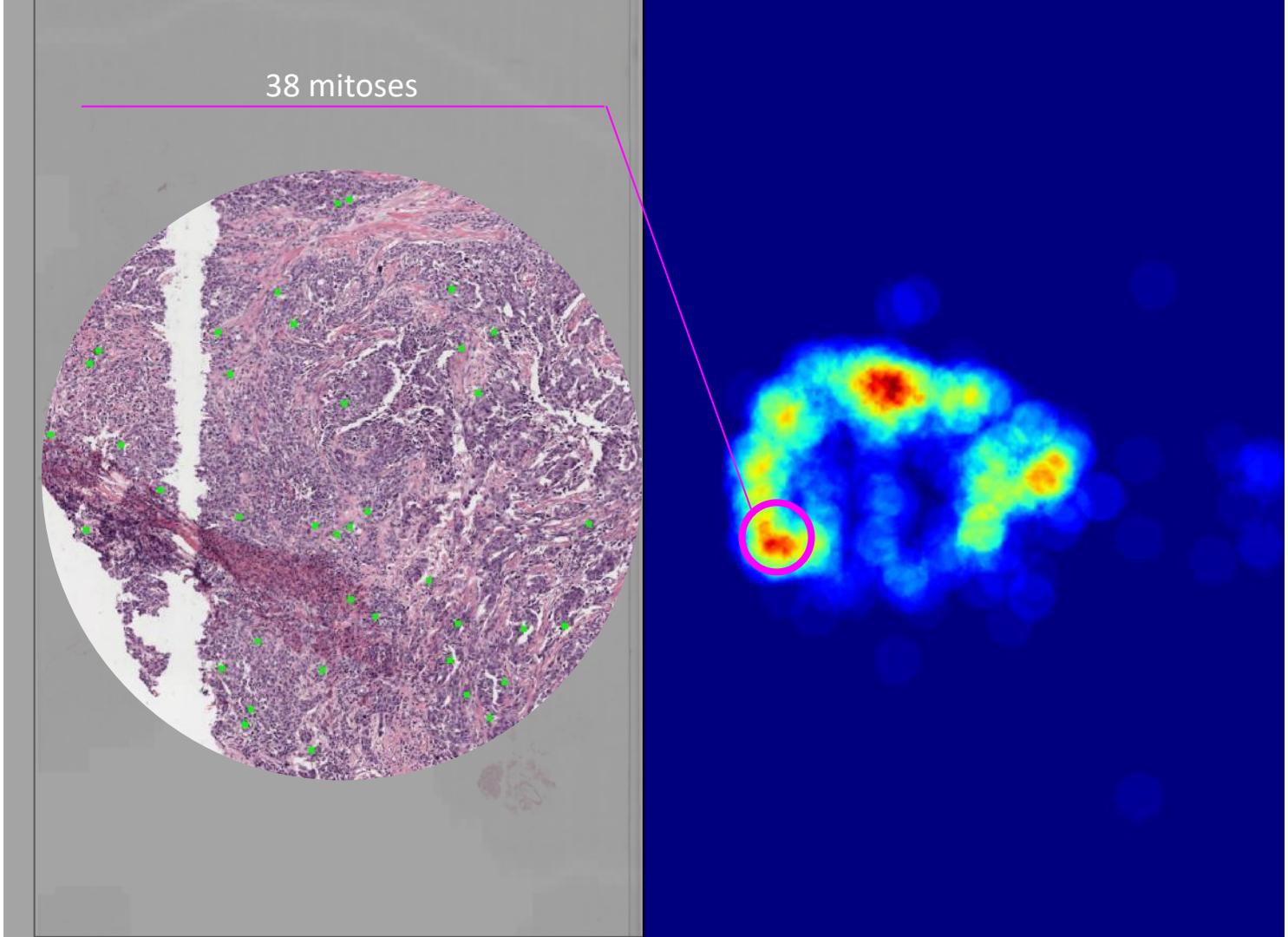
Mitosedichtheid



56 mitoses



Directe zichtbaarheid hot-spots


38 mitoses

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Identificatie van tumor-geassocieerd stroma

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Annals of Oncology

original articles

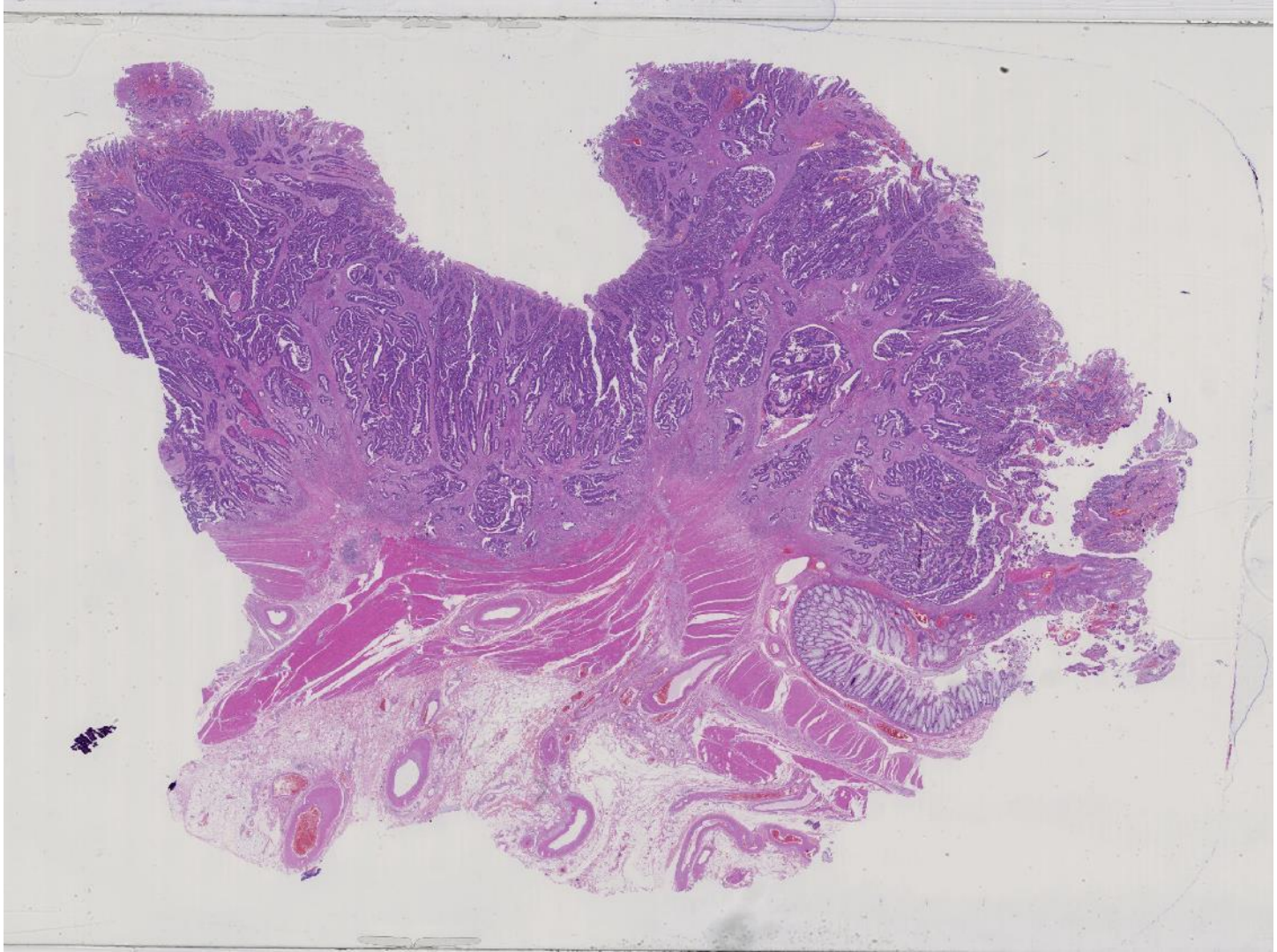
Annals of Oncology 24: 179–185, 2013
doi:10.1093/annonc/mds246
Published online 2 August 2012

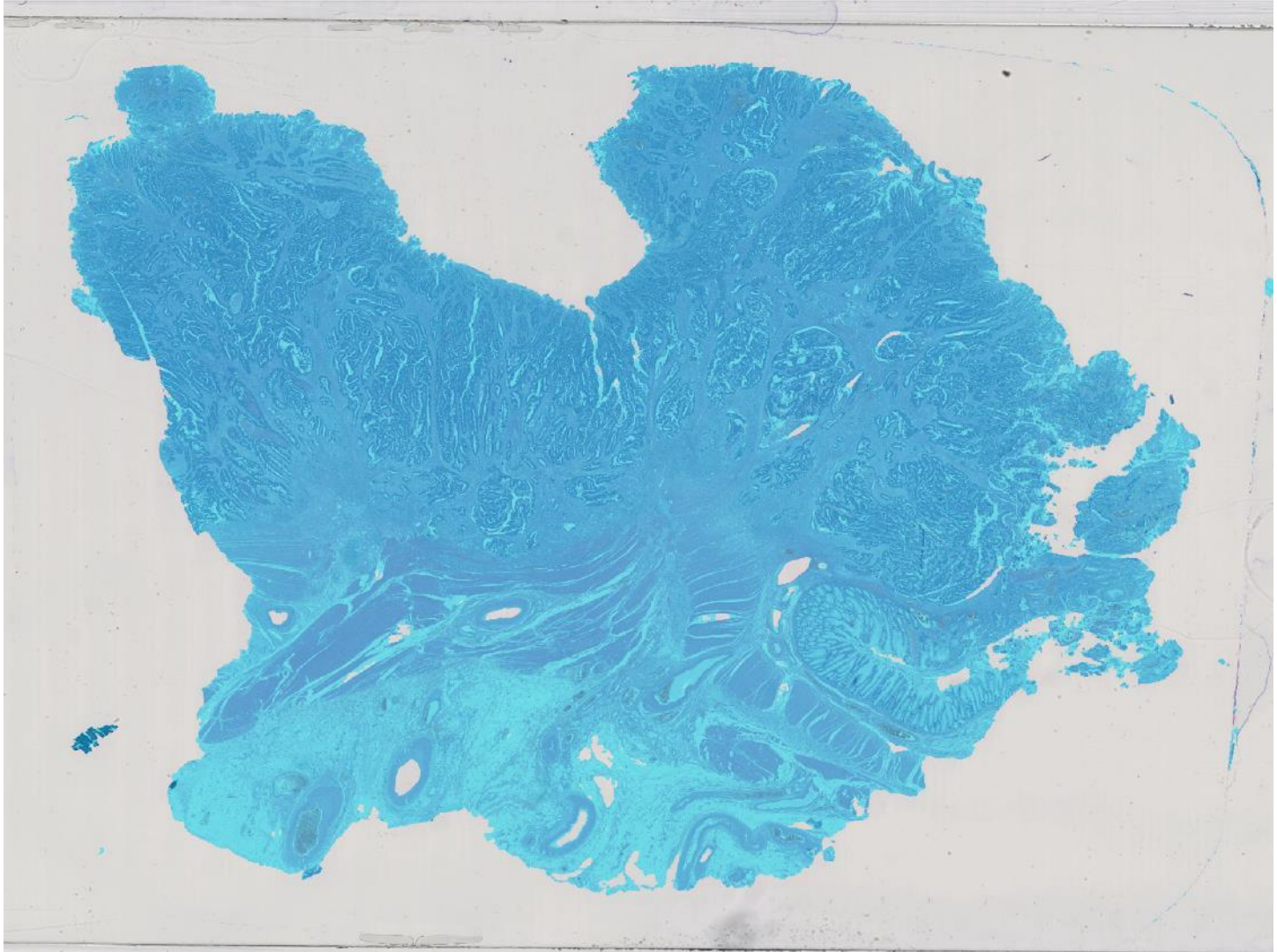
The proportion of tumor-stroma as a strong prognosticator for stage II and III colon cancer patients: validation in the VICTOR trial

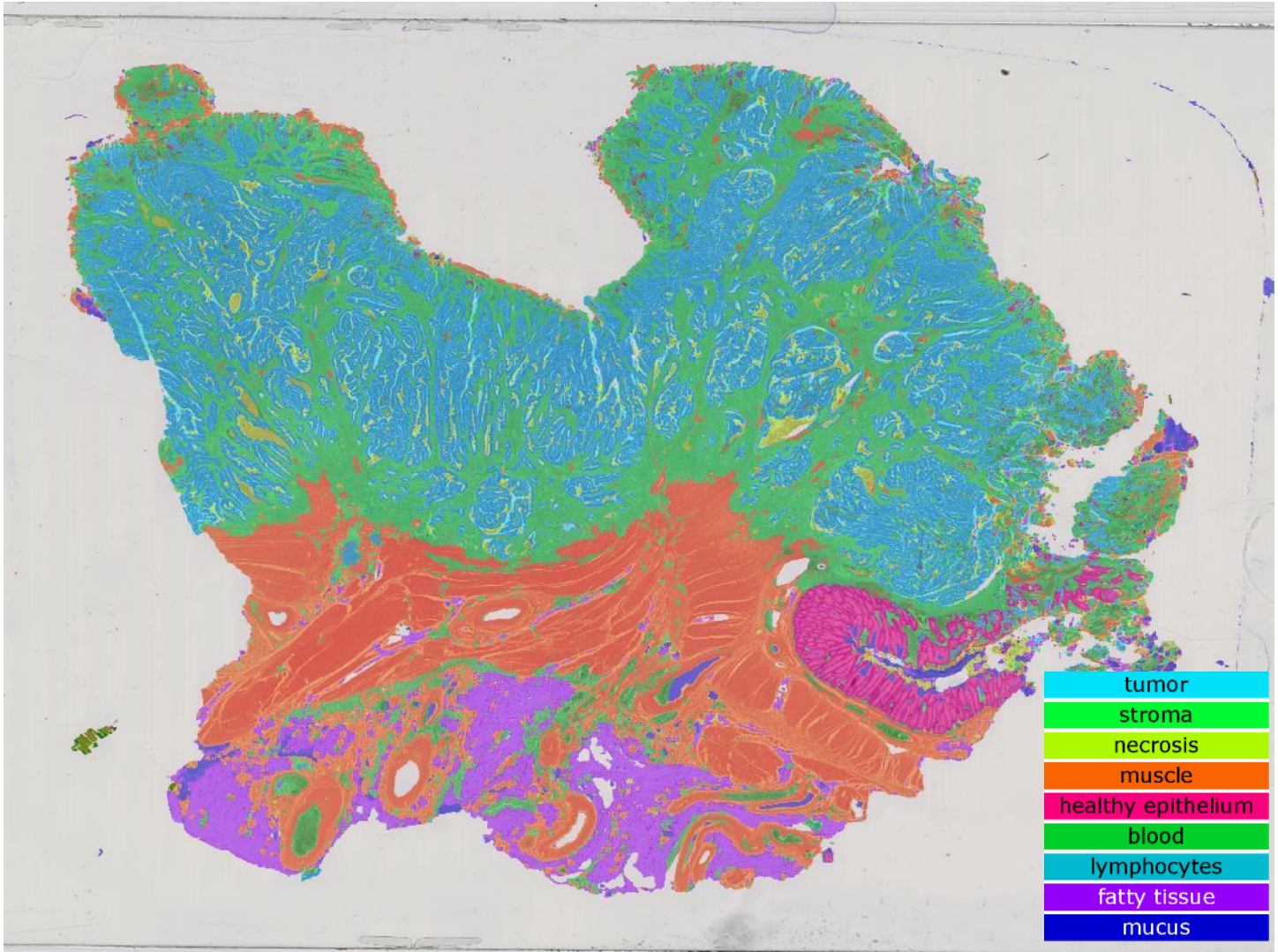
A. Huijbers[1], R. A. E. M. Tollenaar[1], G. W. v Pelt[1], E. C. M. Zeestraten[1], S. Dutton[3], C. C. McConkey[6], E. Domingo[7], V. T. H. B. M. Smit[2], R. Midgley[4], B. F. Warren[8], E. C. Johnstone[4], D. J. Kerr[5] & W. E. Mesker[1]*

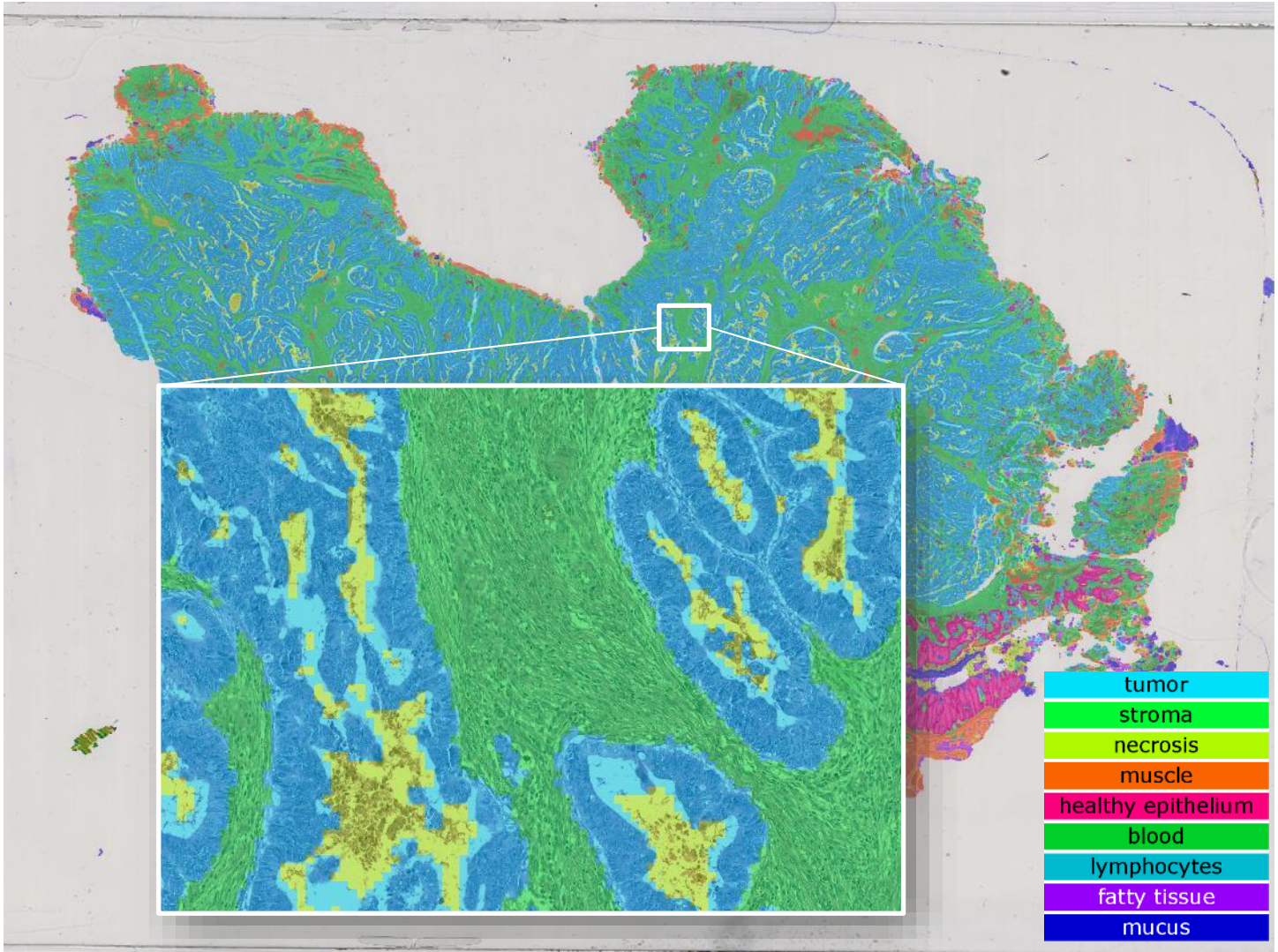
Departments of [1]Surgery; [2]Pathology, Leiden University Medical Center (LUMC), Leiden, The Netherlands; [3]Centre for Statistics in Medicine, University of Oxford, Oxford; Departments of [4]Oncology; [5]Clinical Pharmacology, University of Oxford, Oxford; [6]Clinical Trials Unit, University of Warwick, Coventry; [7]Molecular and Population Genetics, Wellcome Trust Center for Human Genetics, Oxford; [8]Department of Pathology, John Radcliffe Hospital, Headington, Oxford, UK

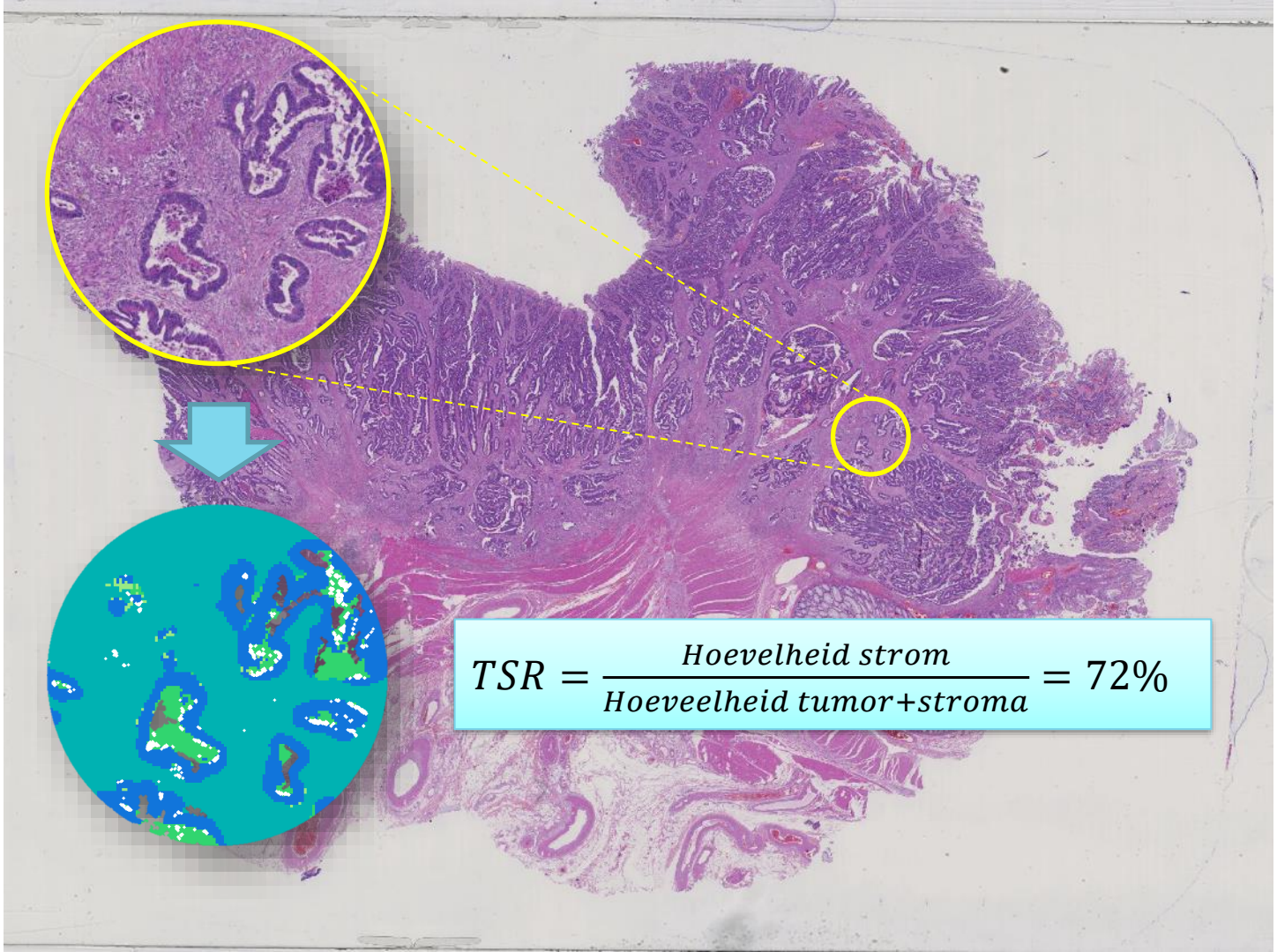
Received 28 February 2012; revised 15 June 2012; accepted 18 June 2012






tumor
stroma
necrosis
muscle
healthy epithelium
blood
lymphocytes
fatty tissue
mucus


tumor
stroma
necrosis
muscle
healthy epithelium
blood
lymphocytes
fatty tissue
mucus

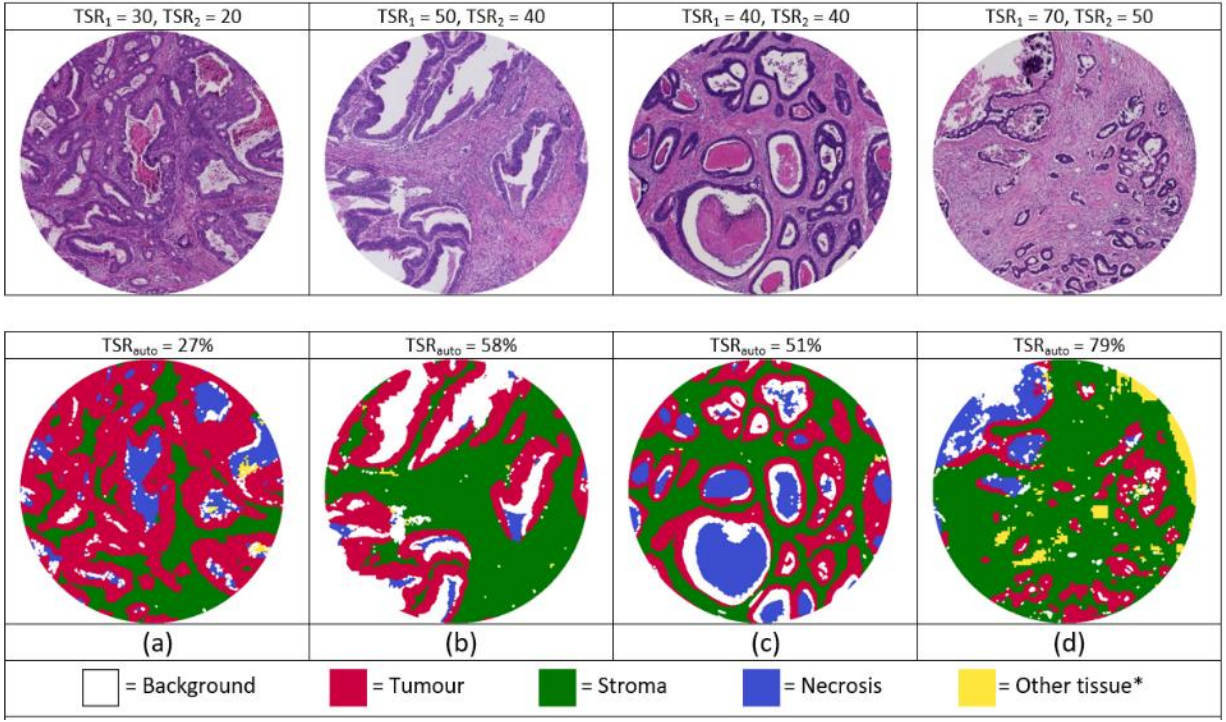

$TSR = \frac{Hoevelheid\ strom}{Hoeveelheid\ tumor+stroma} = 72\%$

Kwantificatie van tumor/stroma-ratio

125 patienten met rectumcarcinoom

- Stadium I-III
- Minimaal 5 jaar follow-up
- Geen neoadjuvante therapie

Kwantificatie van tumor/stroma-ratio

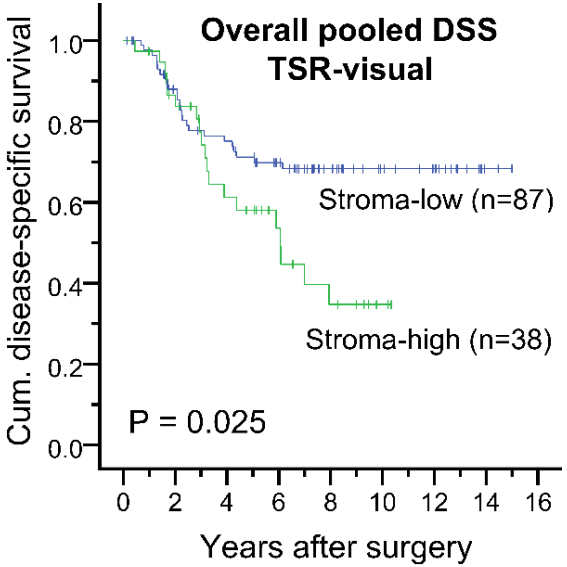


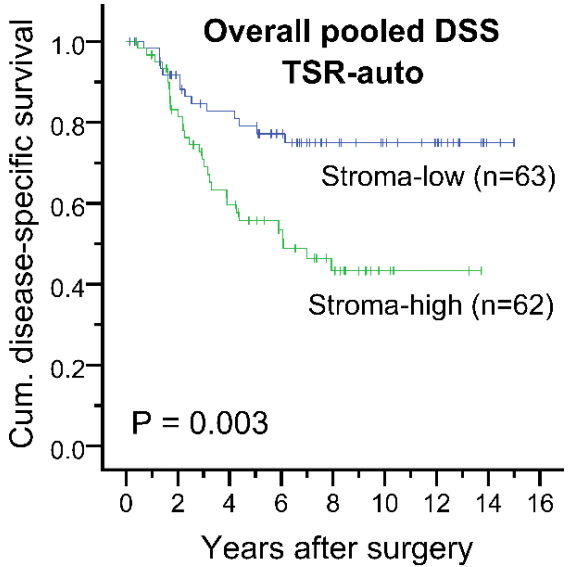
Kwantificatie van tumor/stroma-ratio

Crosstab: Observer 1 versus Observer 2				
κ = 0.548		Observer 2		
		Stroma-low	Stroma-high	Total
Observer 1	Stroma-low	75	8	83
	Stroma-high	16	26	42
	Total	91	34	125

Crosstab: TSR-Visual (consensus) versus TSR-auto				
κ = 0.518		TSR-auto		
		Stroma-low	Stroma-high	Total
TSR-visual (consensus)	Stroma-low	60	27	87
	Stroma-high	3	35	38
	Total	63	62	125

Kwantificatie van tumor/stroma-ratio





Kwantificatie van tumor/stroma-ratio

Table 5. Uni- and multivariate Cox regression analysis for disease-specific survival.

	Univariate analysis		Multivariate analysis			
			Visual		Auto	
	HR (95% CI)	P-val.	HR (95% CI)	P-val.	HR (95% CI)	P-val.
Age	1.01 (0.98-1.04)	0.376				
Gender	0.85 (0.45-1.60)	0.604				
T-stage	2.42 (1.47-3.99)	**0.001**	1.97 (1.16-3.34)	**0.012**	2.05 (1.24-3.38)	**0.005**
N-stage	2.16 (1.49-3.14)	**0.0001**	2.06 (1.13-3.75)	**0.018**	2.12 (1.17-3.84)	**0.014**
Surgical procedure	1.48 (0.94-2.31)	0.090				
Tumour grade	2.96 (1.42-6.17)	**0.004**	2.40 (1.05-5.48)	**0.038**	2.23 (0.99-5.00)	0.052
Adj. chemoth.	1.17 (0.28-4.82)	0.831				
Adj. radioth.	2.56 (1.41-4.63)	**0.002**	0.72 (0.27-1.88)	0.496	0.68 (0.27-1.72)	0.417
TSR-visual	1.96 (1.08-3.58)	**0.027**	2.07 (1.09-3.93)	**0.026**		
TSR-auto	2.57 (1.36-4.86)	**0.004**			2.75 (1.44-5.27)	**0.002**

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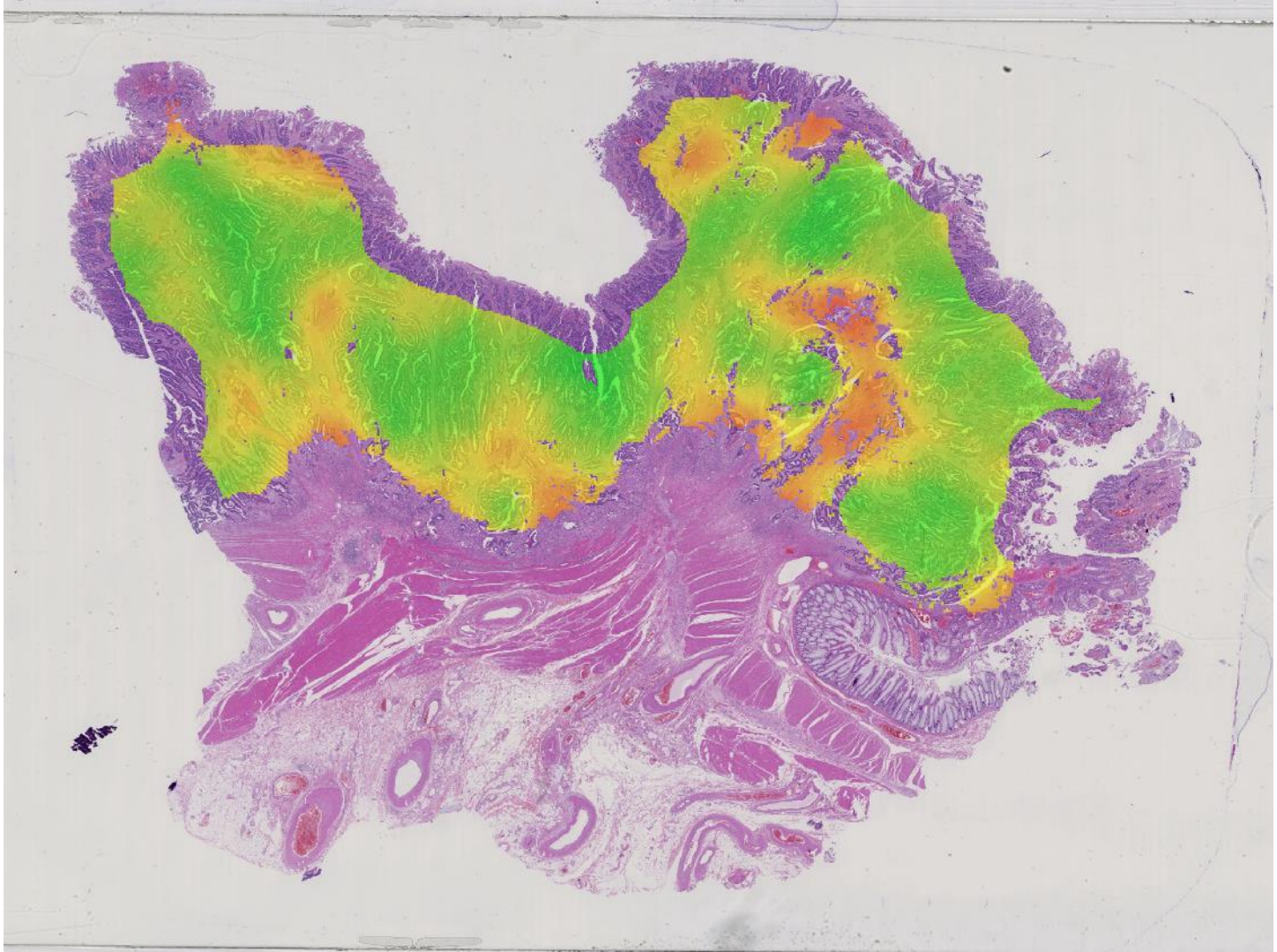


Zelflerende computers in de pathologie

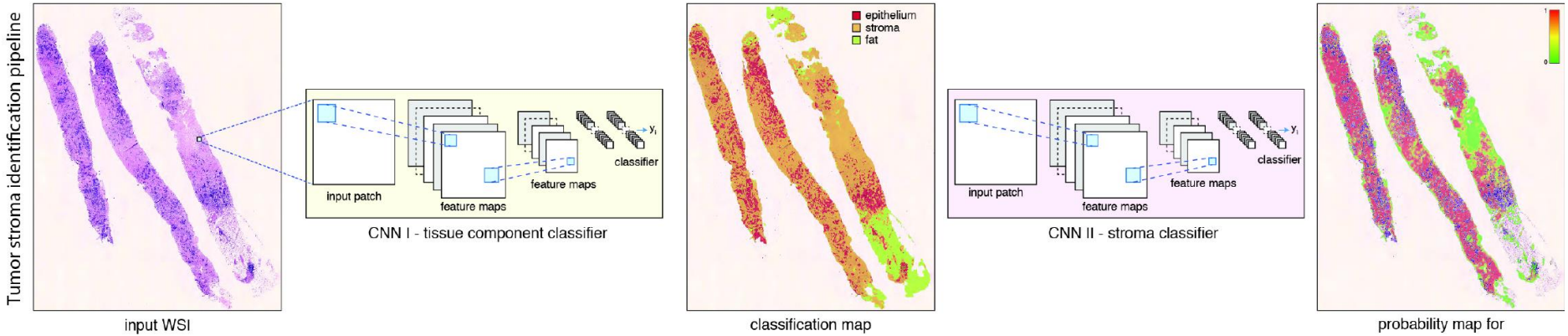
Detectie van metastasen in lymfeklieren

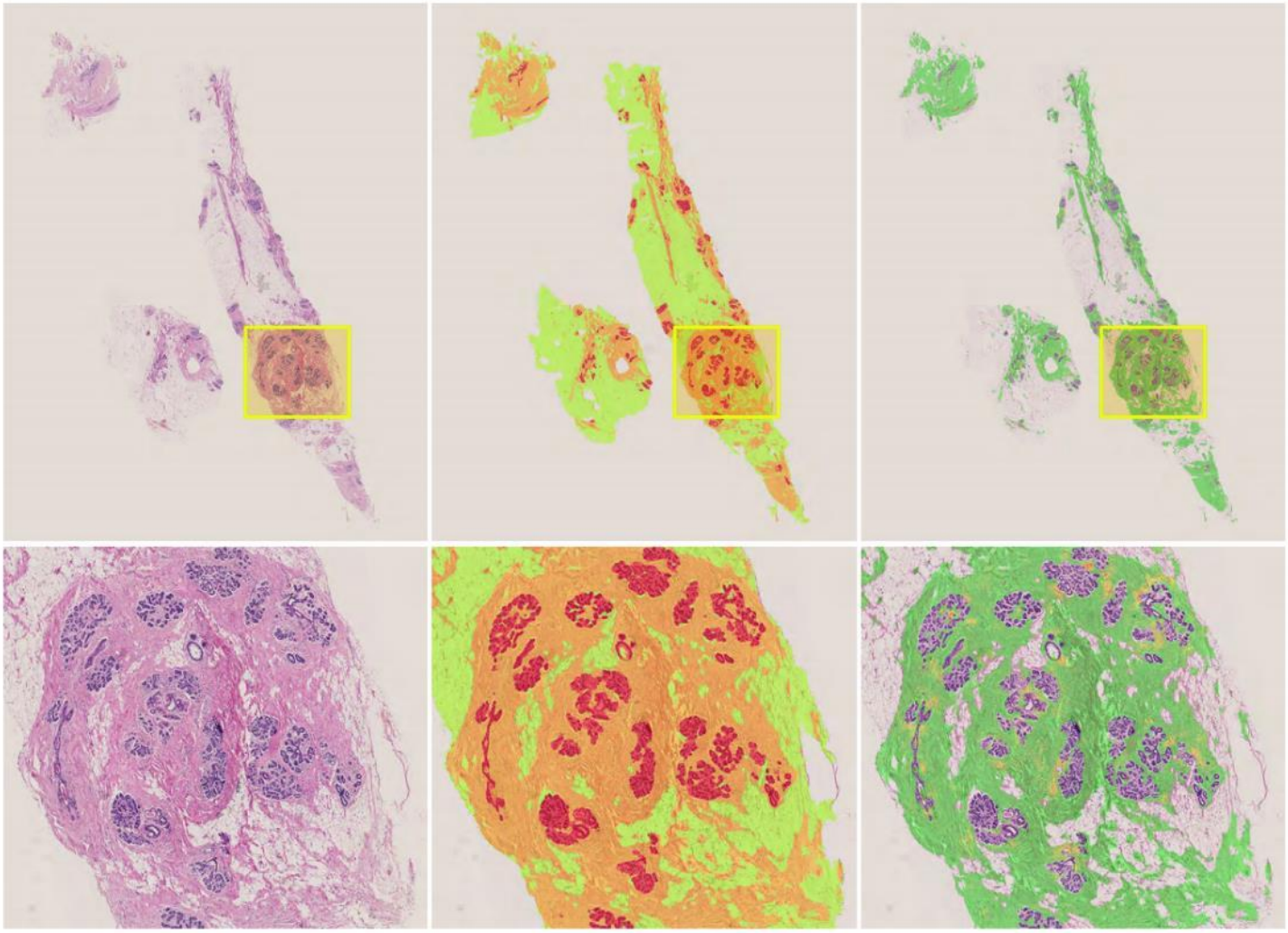
Automatisch tellen van mitoses

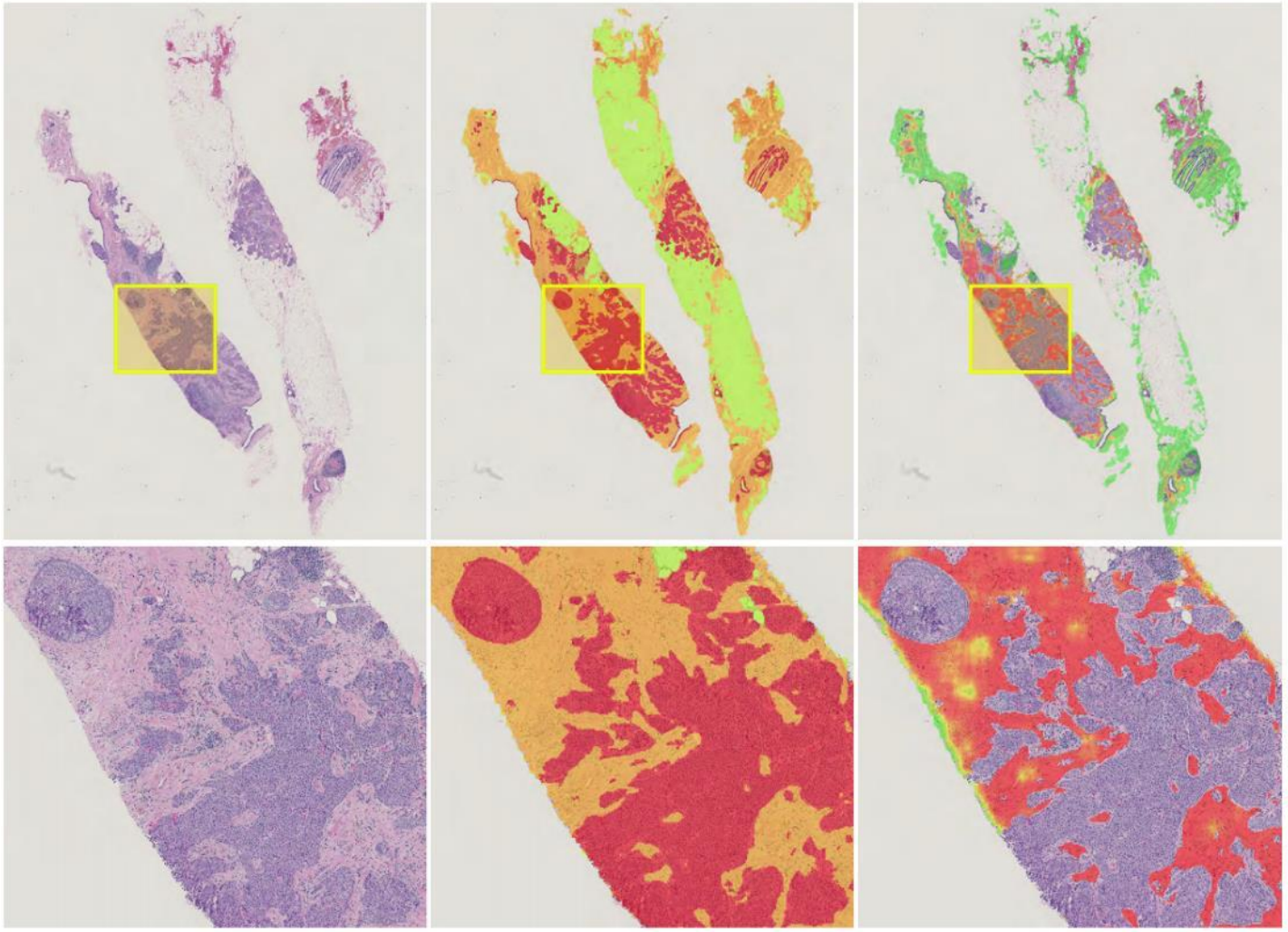
Kwantificatie van tumor/stroma-ratio

Identificatie van tumor-geassocieerd stroma

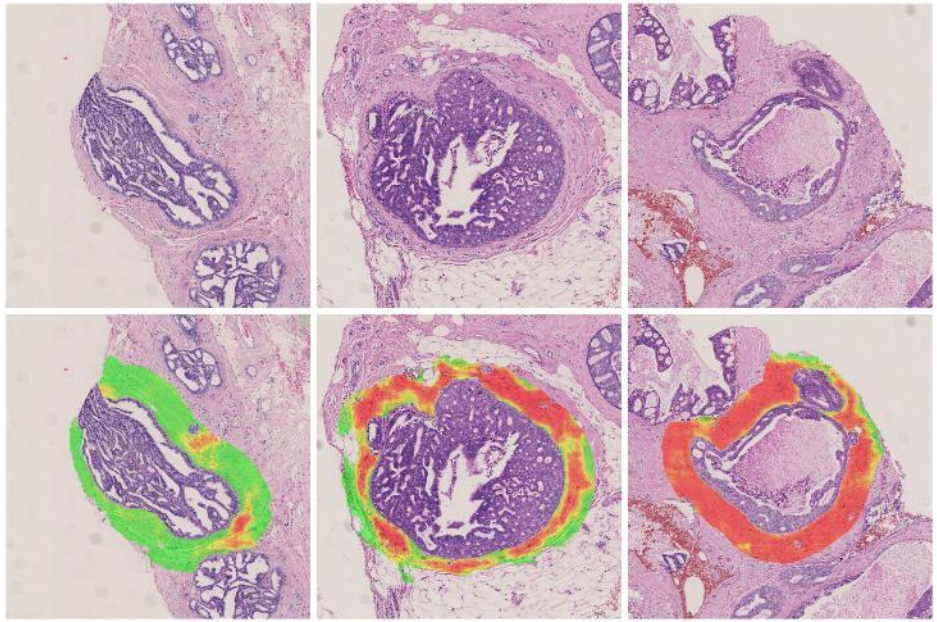
Tumor-geassocieerd stroma

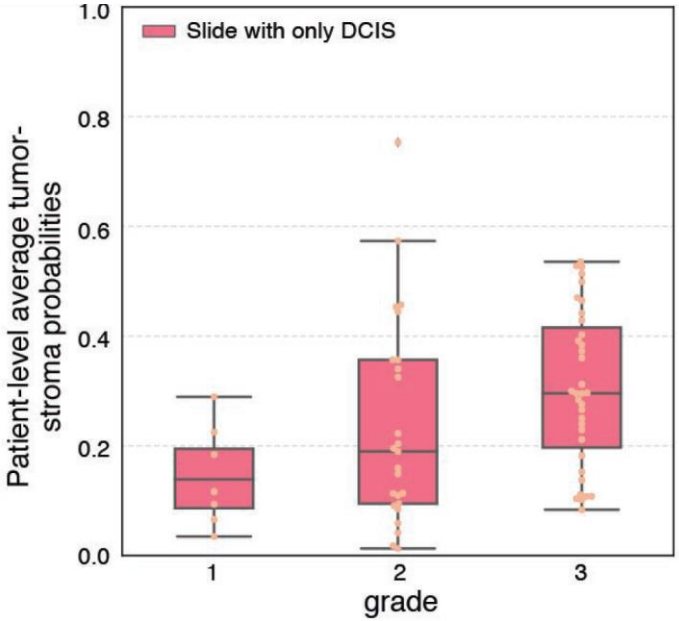




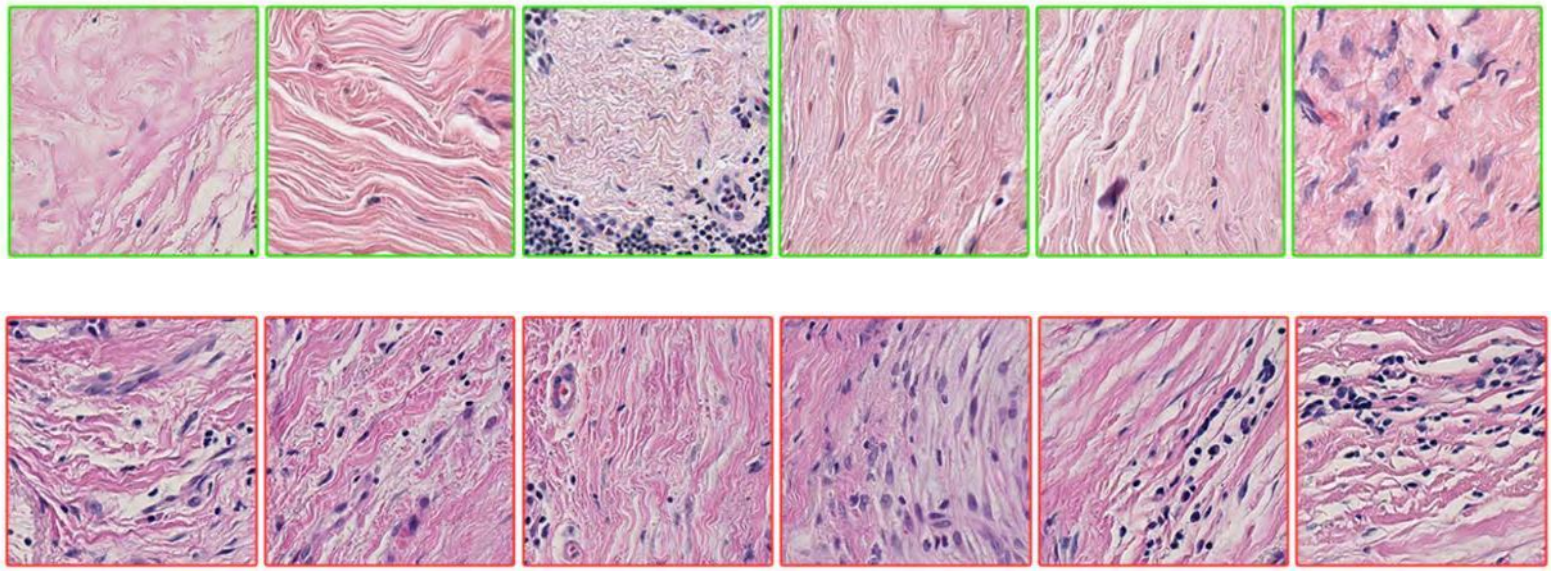


Tumor-geassocieerd stroma





Tumor-geassocieerd stroma



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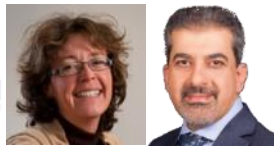

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TU/e

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SEVENTH FRAMEWORK
PROGRAMME


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