Künstliche Intelligenz (KI) im hämatologisch/onkologischen Alltag: was ist schon möglich?

Claudia Haferlach

MLL- Münchner Leukämielabor

Offenlegung Interessenskonflikte Claudia Haferlach

1. Anstellungsverhältnis oder Führungsposition

MLL – Münchner Leukämielabor

2. Beratungs- bzw. Gutachtertätigkeit

-

3. Besitz von Geschäftsanteilen, Aktien oder Fonds

MLL – Münchner Leukämielabor

4. Patent, Urheberrecht, Verkaufslizenz

-

5. Honorare

-

6. Finanzierung wissenschaftlicher Untersuchungen

-

7. Andere finanzielle Beziehungen

-

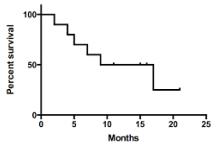
8. Immaterielle Interessenkonflikte

-

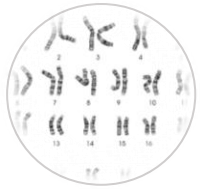
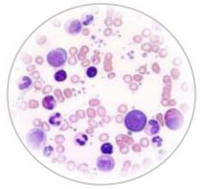
Agenda

Grundsätzliches

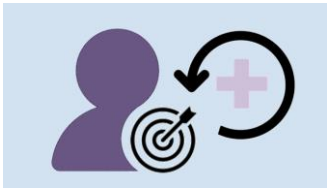
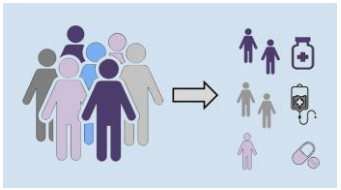
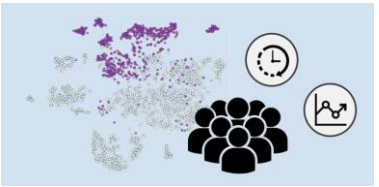




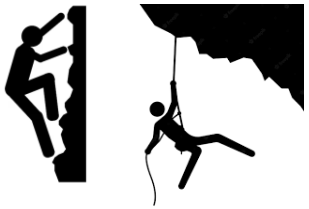

Überblick über Einsatzgebiete in der Hämatologie

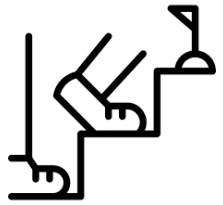
Diagnostische Projekte im Detail

Weitere Einsatzoptionen in der Hämatologie

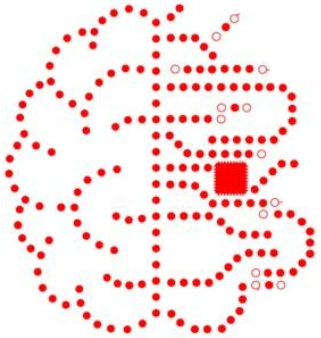


Herausforderungen



Nächste Schritte

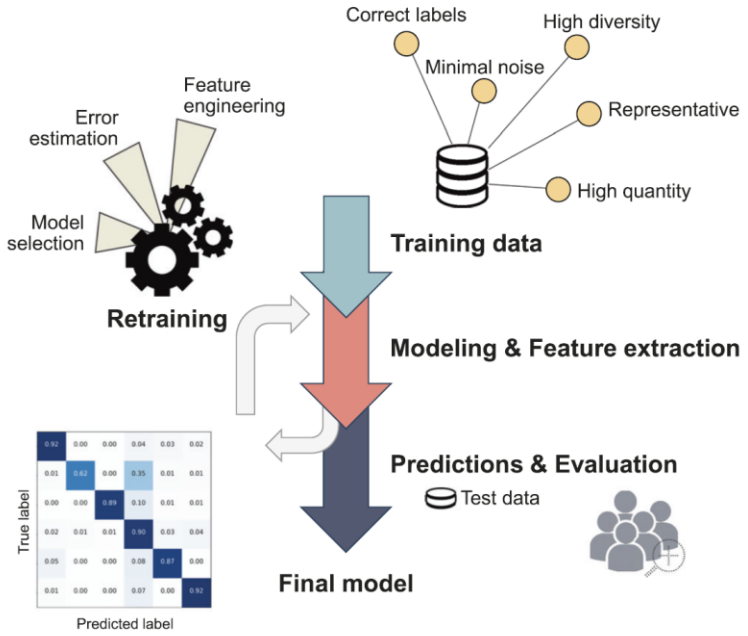
Grundsätzliches



KI kein Selbstzweck

die richtige Frage stellen
geeignete Fragestellung auswählen
genaue Beschreibung des Ziels

Geeignetes
Werkzeug aus dem
KI Werkzeugkasten
auswählen



Model erstellen
Model testen
prospektiv validieren

vor der Validierung festlegen: was ist die „Wahrheit“ / der Goldstandard und warum?

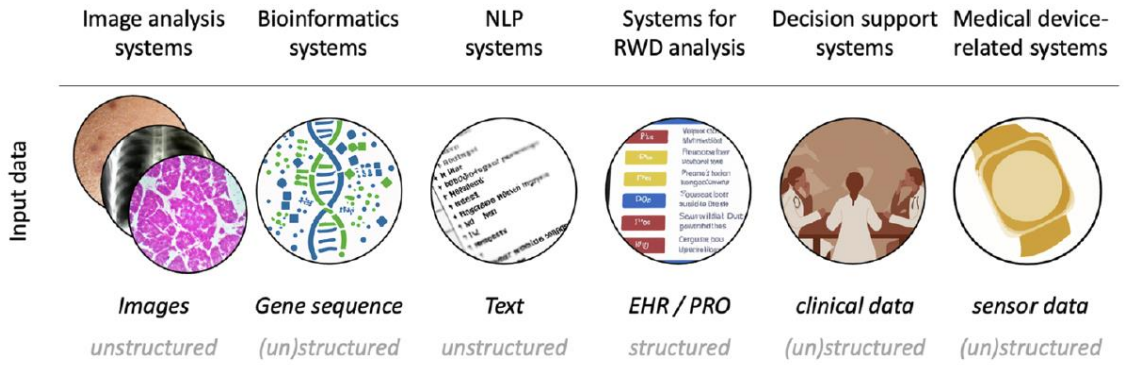
Grundsätzliches zu Methoden

Machine Learning
Techniken, die anhand von Beispielen lernen anstatt mit definierten Regeln zu arbeiten

Natural Language Processing
Fähigkeit, menschliche Sprache und unstrukturierten Text in maschinenlesbare strukturierte Daten umzuwandeln, die die Absicht der Sprache zuverlässig wiedergeben

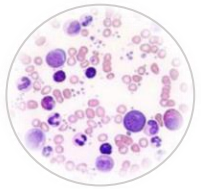
Übersichtsartikel des Arbeitskreises Künstliche Intelligenz der DGHO

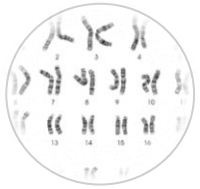
An overview and a roadmap for artificial intelligence in hematology and oncology
Journal of Cancer Research and Clinical Oncology (2023) 149:7997–8006



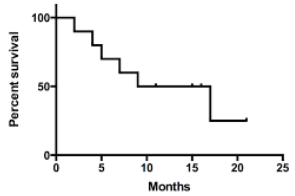
Anwendungen von KI in der Hämatologie

- Diagnostik





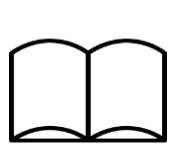
- Prognose-Einschätzung



- Therapie-Planung

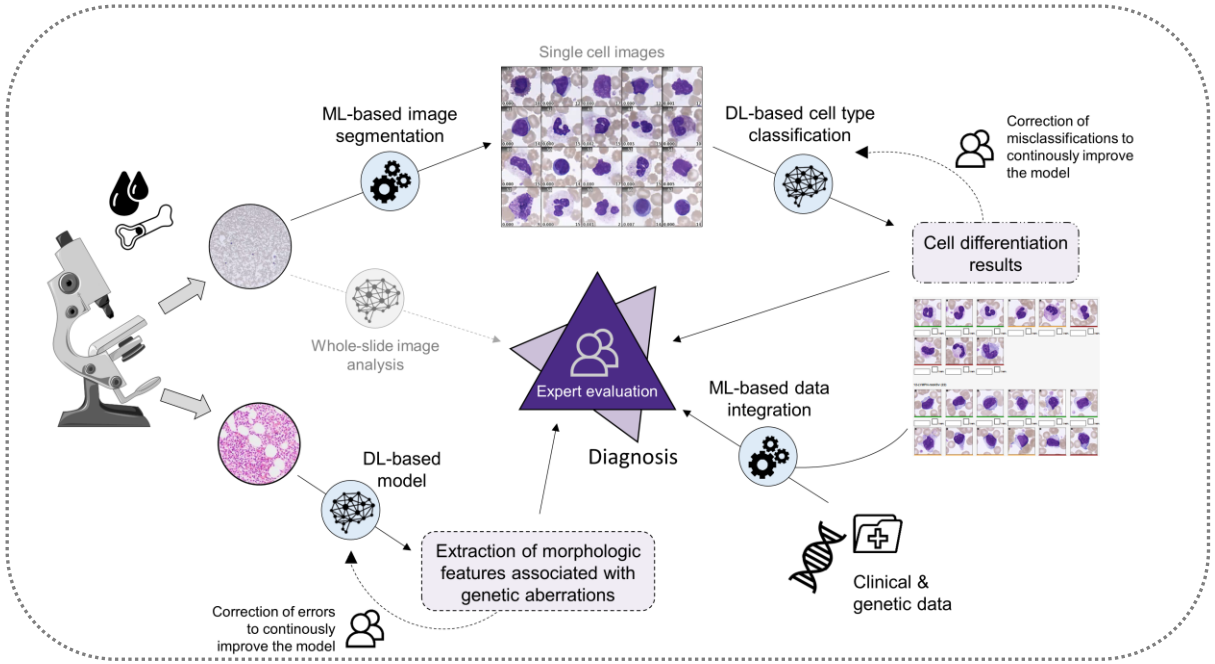
- Therapie-Überwachung

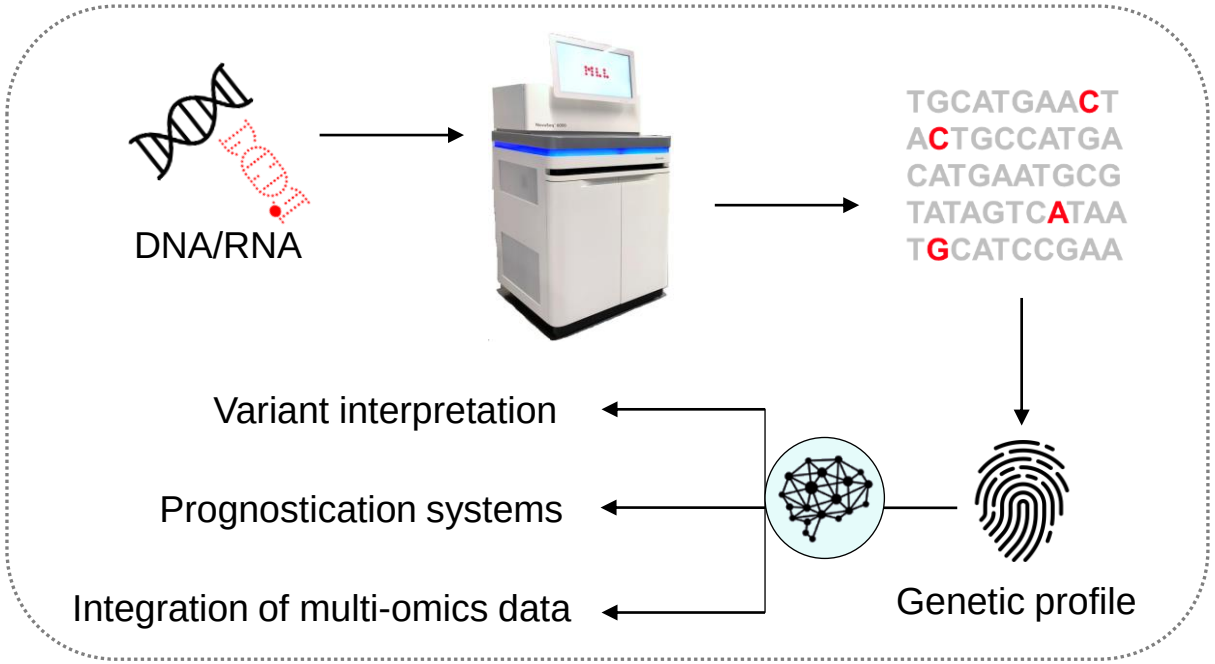
- Unterstützung bei klinischen Entscheidungen durch Aufbereitung von Wissen

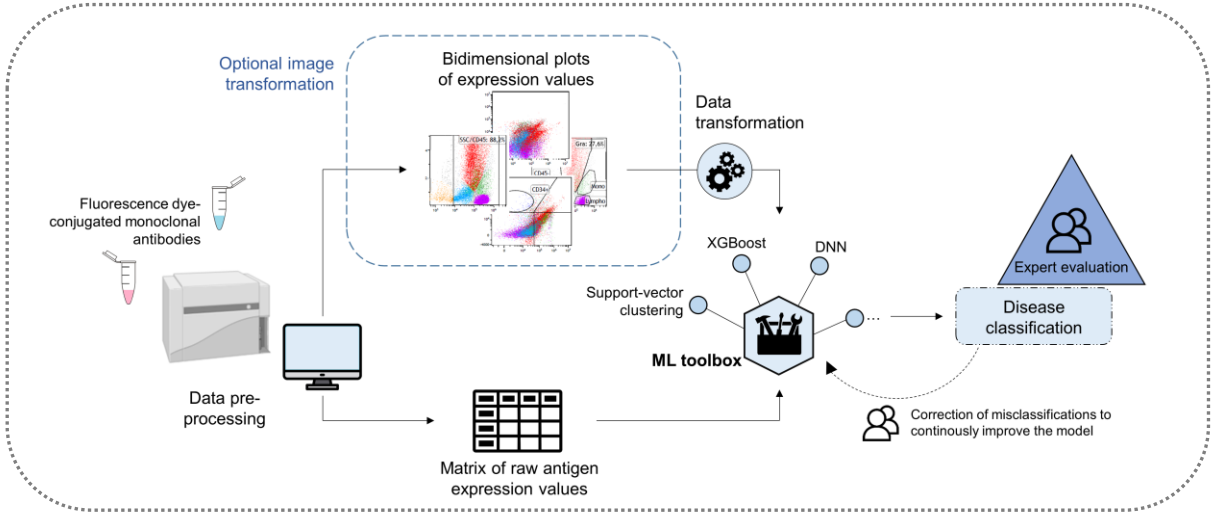


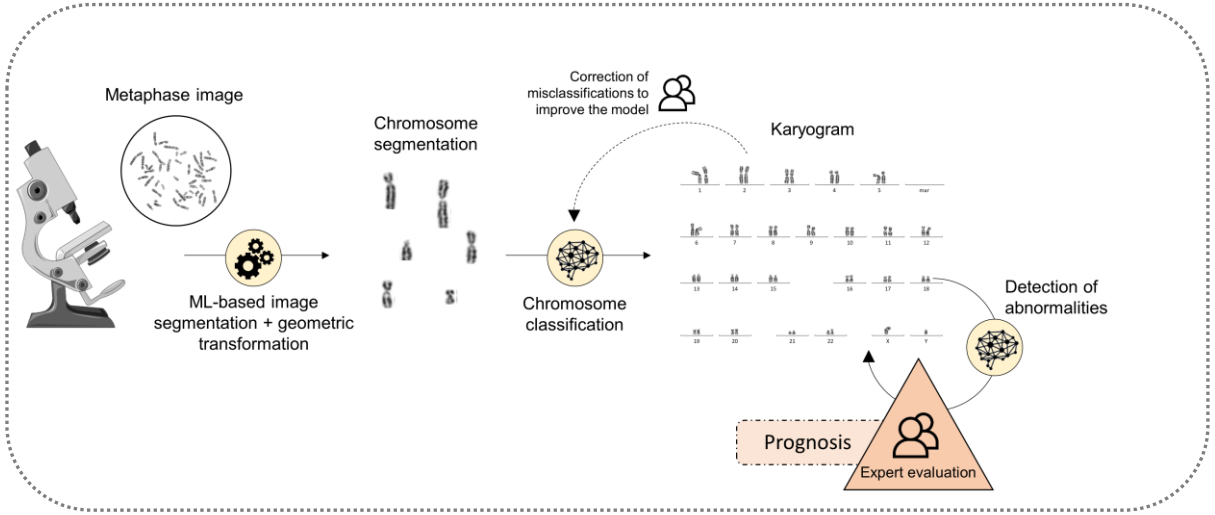
- Automatisierung von administrativen Prozessen

Unterstützung in der Diagnostik durch KI







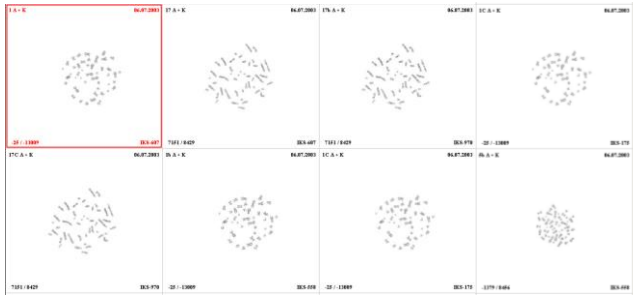


W. Walter et al. Blood Reviews 2022

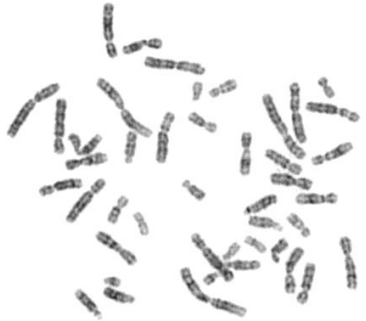
Unterstützung in der Diagnostik durch KI - Beispiel Chromosomenanalyse

Workflow

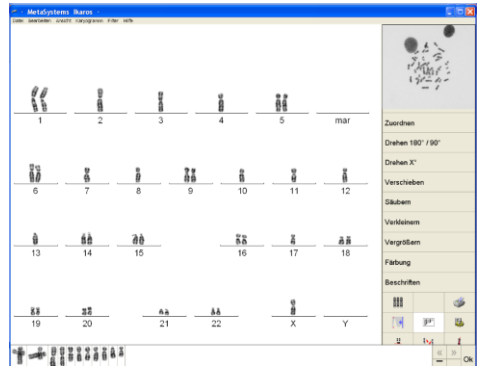
At least 20 metaphases have to be selected and analyzed



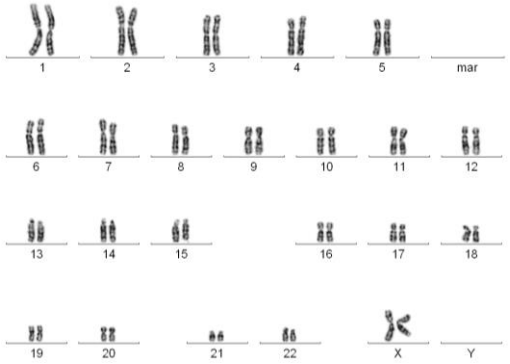
Chromosomes have to be separated



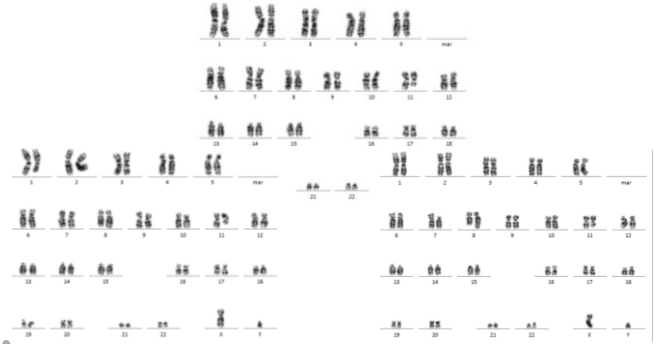
have to be sorted



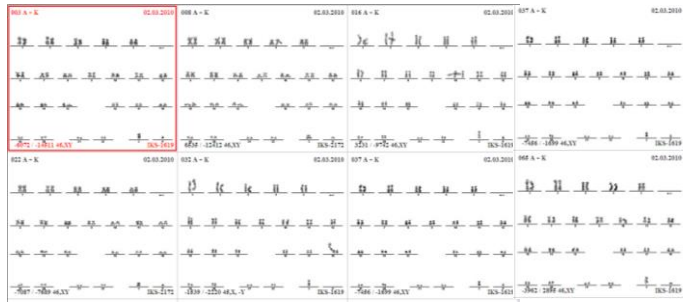
Karyotype has to be analyzed



Clonal abnormalities to be identified or excluded

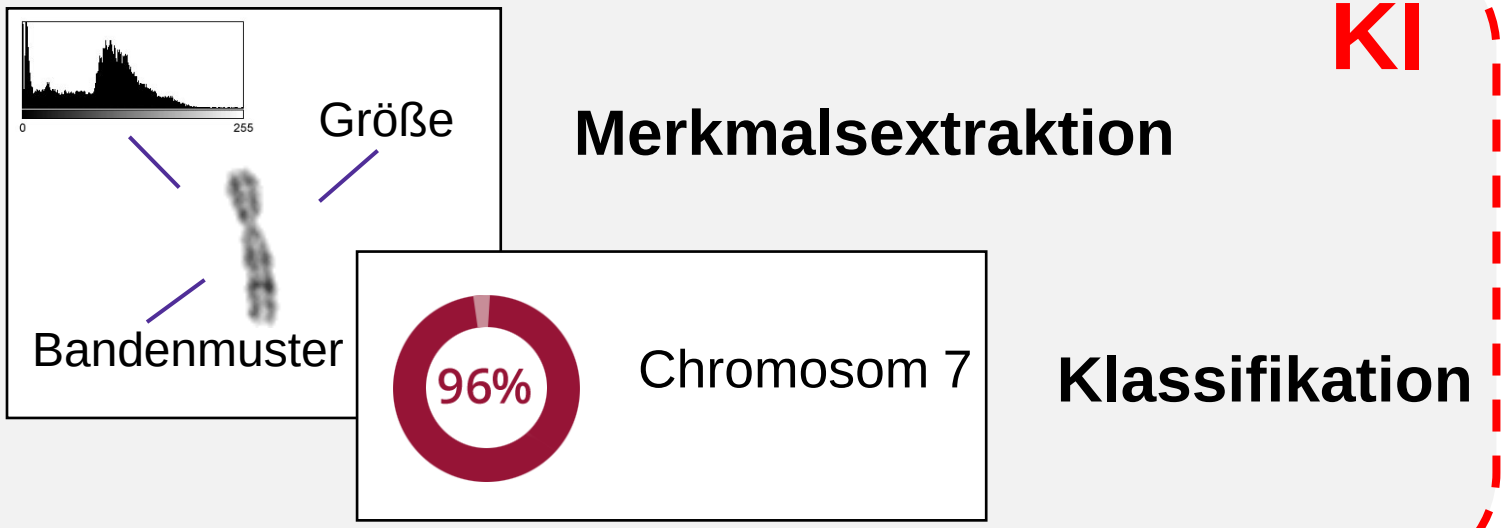


Final result based on at least 20 karyograms



KI ist besonders weit entwickelt in der Bilderkennung

Was sind die grundlegenden Schritte?



Training

Validierung

- Decision Trees
- Support Vector Machines
- Neuronale Netze
- Bayes-Klassifikator
- Logistic Regression
- Reinforcement Learning

Training data set:

- to build the model
- adjust the parameters to optimize accuracy of predictions

Validation data set:

- evaluate a model fit on the training dataset, tuning model hyperparameters

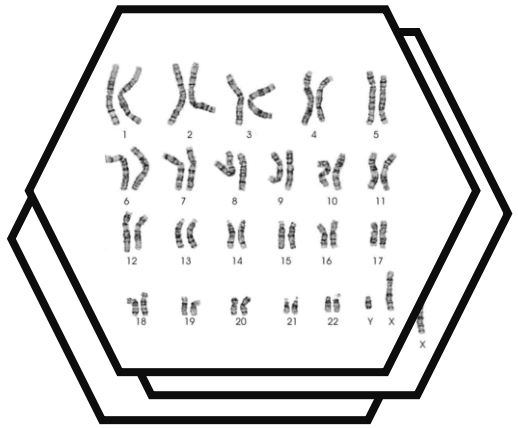
Test data set:

- to provide an unbiased evaluation of the final model

Automation of Karyotyping

Building an AI based algorithm – 1st step: classification of normal chromosomes

100,000 unselected manually arranged karyograms with normal karyotype from the digital archive

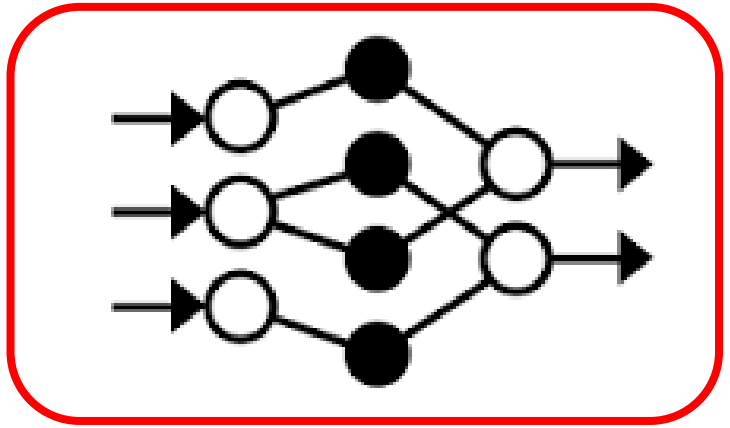


Task 1:
Determine chromosome class
(n=24)

Task 2:
Determine chromosome orientation
(n=360)

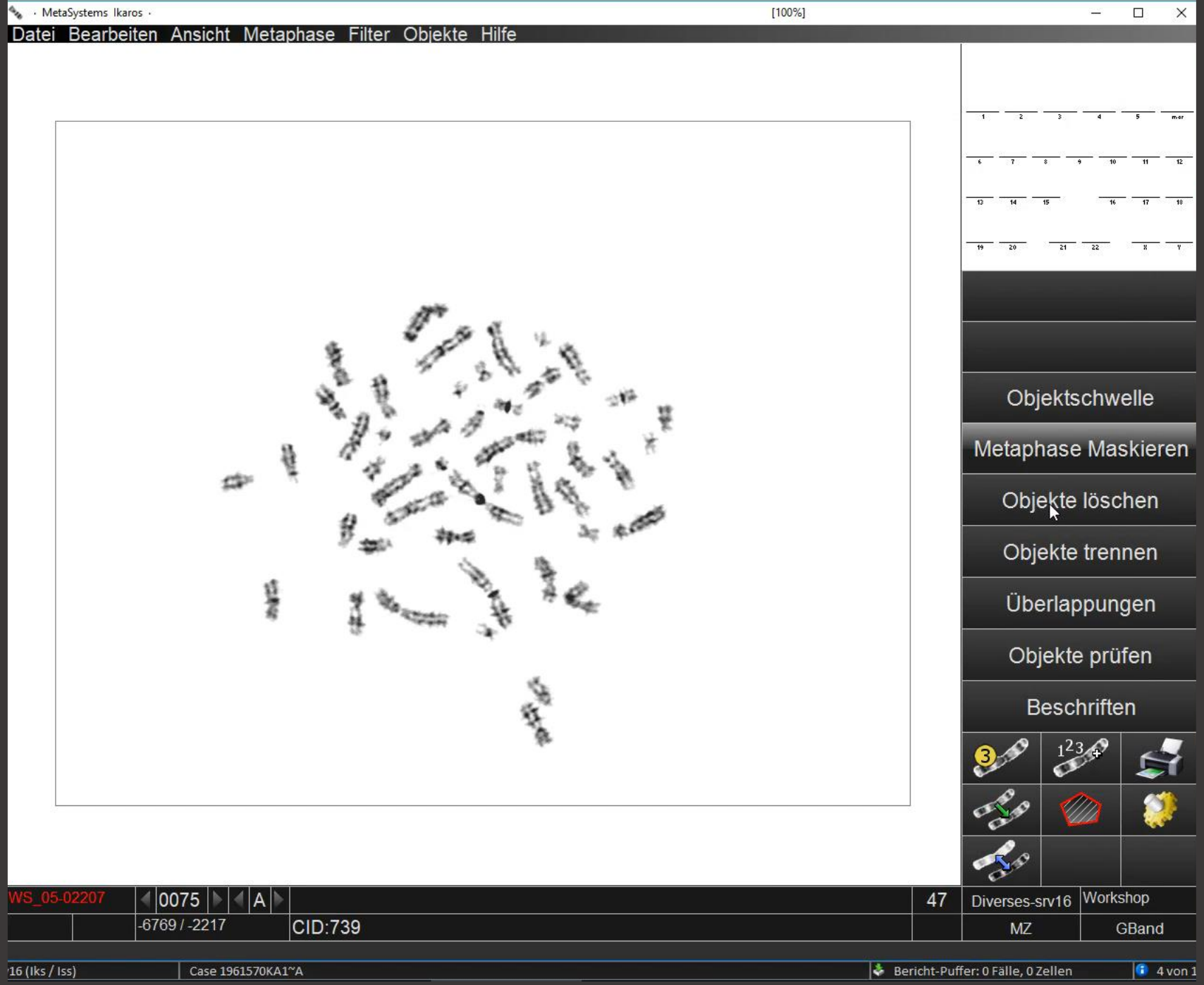
Input: 6 mio. parameters
DNN: two distinct output layers to simultaneously predict chromosome number and angle that is required to rotate the chromosome in its correct, vertical position

DNN: Deep Neural Network

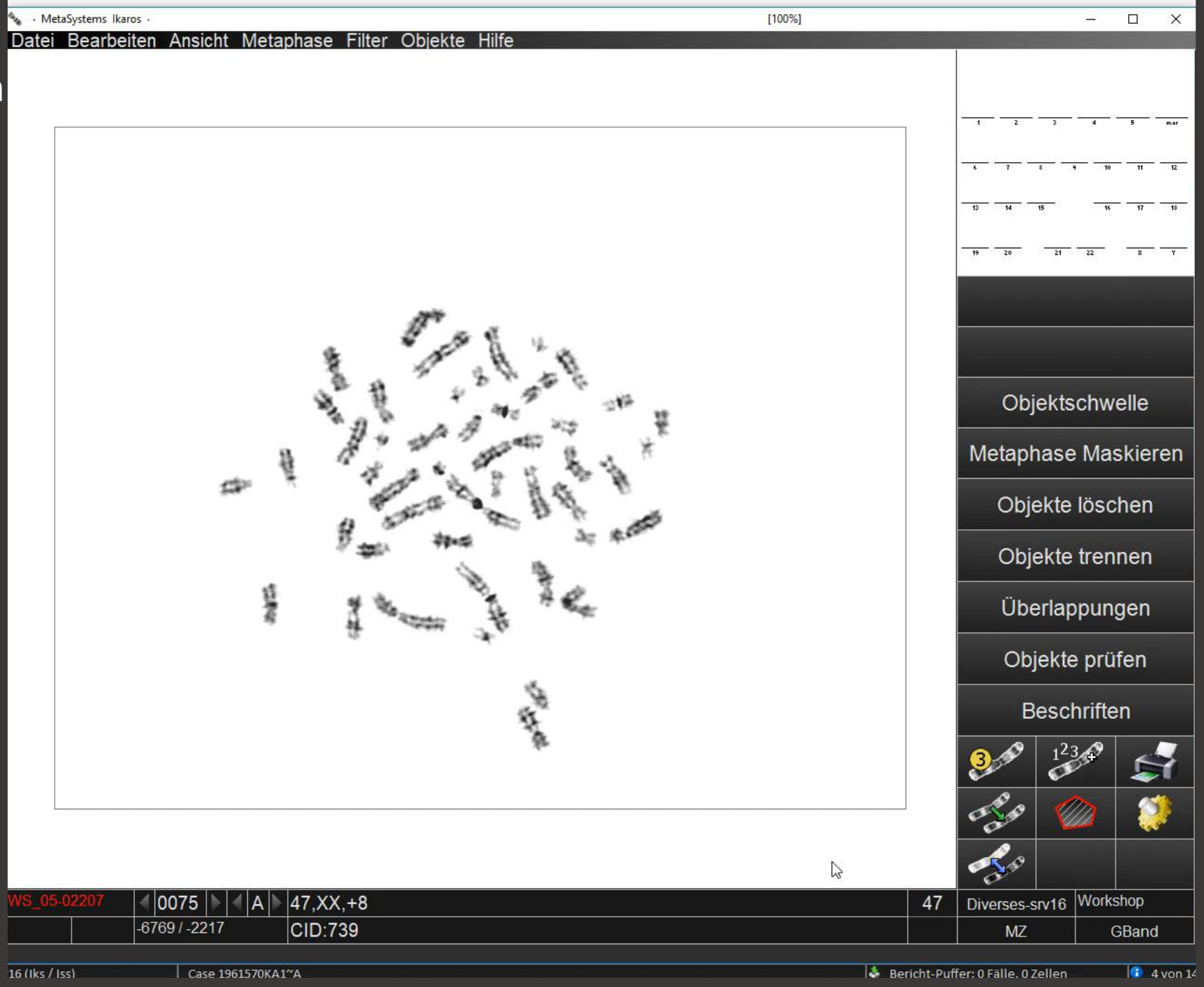


Training of the DNN took 16 days on a Nvidia RTX 2080 Ti graphic card with 4352 cores

Manual karyotyping by a highly experienced technician in real time



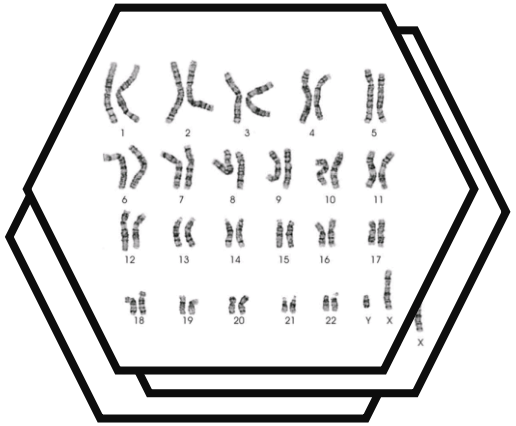
Automated classification based on AI + review by technician



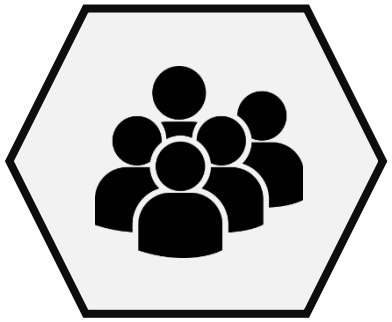
Automation of Karyotyping

AI Classifier for normal chromosomes – Testing results

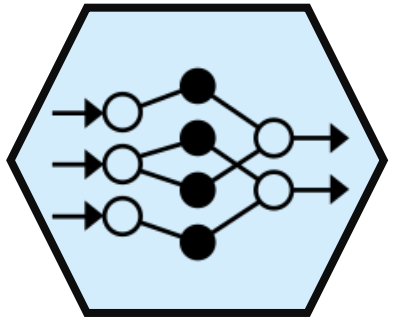
prospective validation
independent set of 500 NKG



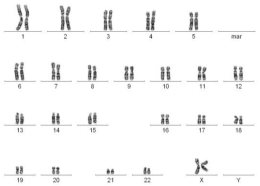
Experts



Deep
Neural Network



Classification agreement
22,675/23,000 chromosomes (98.6%)



Complete agreement on karyogram
369/500 (73.8%)
+ 20% only 2 chromosomes were interchanged

After 7 months of development and intensive testing AI Classifier implemented into routine workflow

Automation of Karyotyping

AI Classifier for normal chromosomes – Misclassification – Disagreement

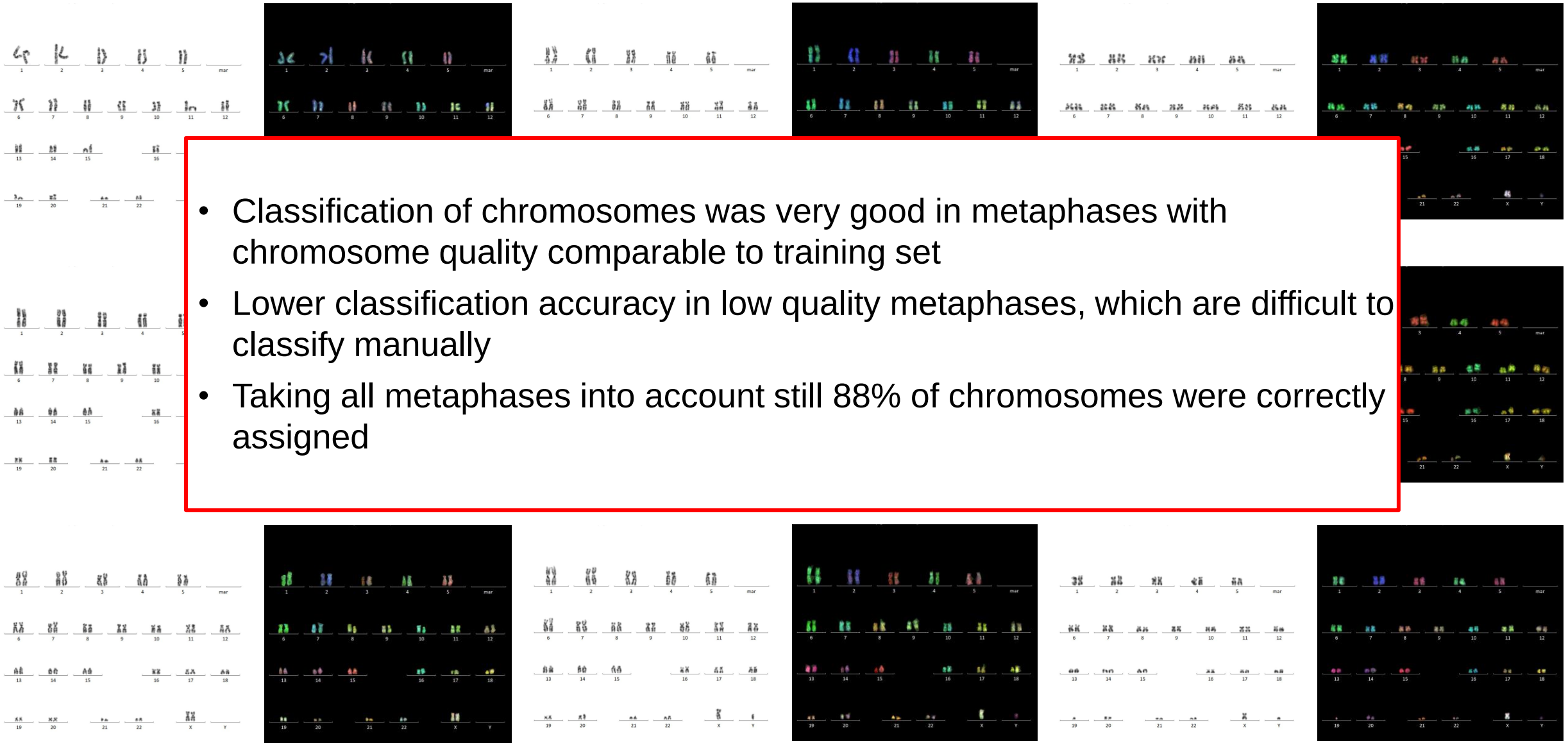
Chromosome class according to expert

Chromosome class according to DNN

	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15	#16	#17	#18	#19	#20	#21	#22	#X	#Y
#1	1000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
#2	0	999	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
#3	0	0	998	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
#4	0	0	0	975	24	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
#5	0	1	0	23	976	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
#6	0	0	0	0	0	995	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
#7	0	0	1	0	0	0	990	0	2	0	1	0	0	0	0	0	0	0	0	0	0	0	6	0
#8	0	0	0	1	0	1	0	982	4	6	0	5	0	0	0	0	0	0	0	0	0	0	1	0
#9	0	0	1	0	0	0	2	1	979	3	5	0	0	0	0	0	0	0	0	0	0	0	5	0
#10	0	0	0	0	0	0	0	8	1	986	1	2	0	0	0	0	0	0	0	0	0	0	0	0
#11	0	0	0	0	0	0	1	0	4	0	992	0	0	0	0	0	0	0	0	0	0	0	0	0
#12	0	0	0	0	0	1	0	1	0	3	0	993	0	0	1	0	0	0	0	0	0	0	0	0
#13	0	0	0	0	0	0	0	0	0	0	1	0	995	1	3	0	0	0	0	0	0	0	0	0
#14	0	0	0	0	0	0	0	0	0	0	0	0	2	958	38	0	0	0	0	1	0	0	0	0
#15	0	0	0	0	0	0	0	0	0	0	0	0	2	38	957	0	0	1	0	0	0	0	0	1
#16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	999	0	1	0	0	0	0	0	0
#17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	993	4	1	1	0	0	0	0
#18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	4	992	0	0	0	0	0	3
#19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	981	9	1	4	0	2
#20	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	8	988	0	0	0	2
#21	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	994	5	0	1
#22	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	0	4	982	0	7
#X	0	0	0	0	0	2	6	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	987	0
#Y	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	0	1	1	5	0	984
n.a.	0	0	0	0	0	1	0	6	5	2	0	0	1	2	0	0	2	1	4	0	0	4	0	0

Validation of AI based automated karyotyping against 24 color FISH

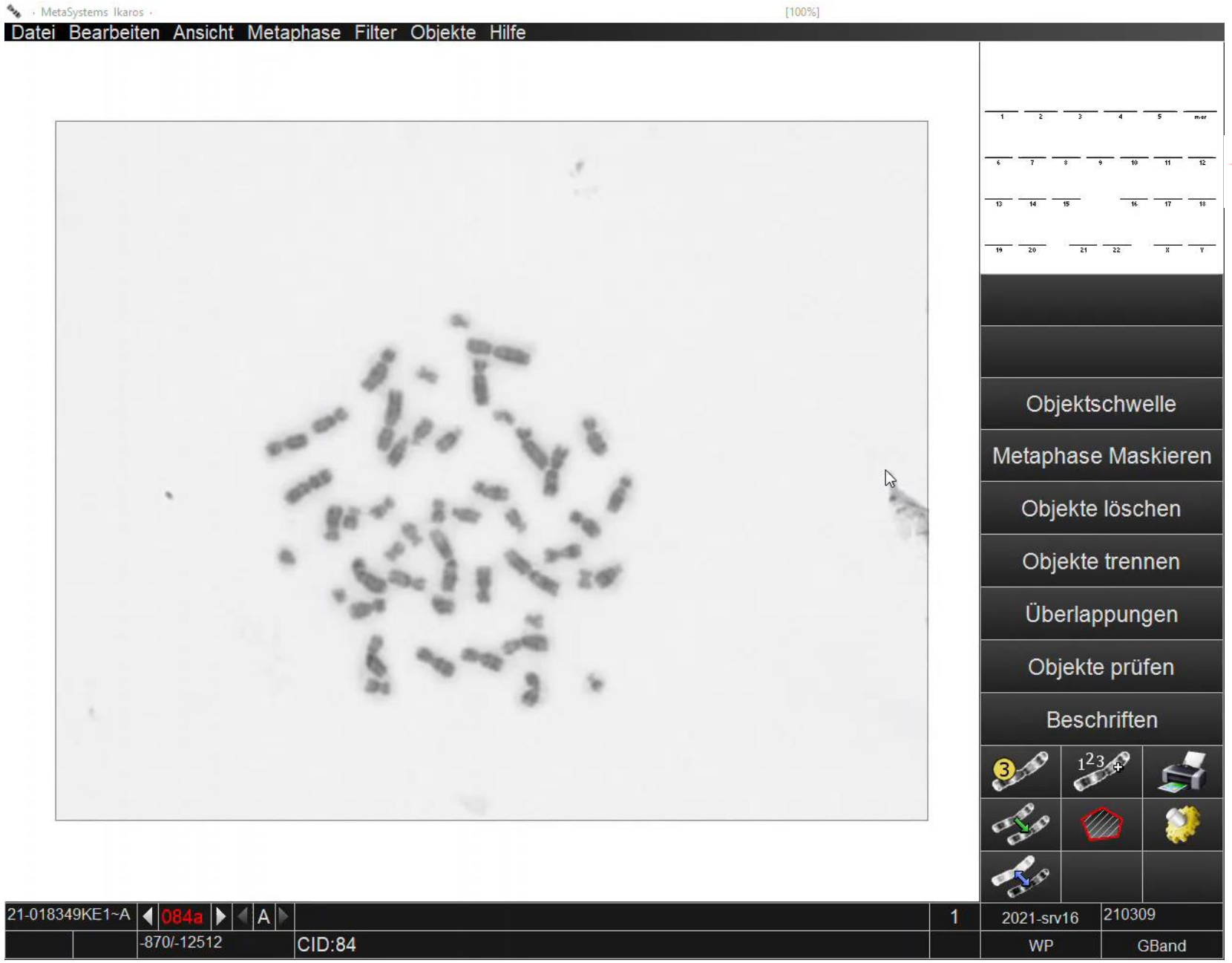
AI based algorithm classified 500 metaphases with a large variety of metaphase quality



- Classification of chromosomes was very good in metaphases with chromosome quality comparable to training set
- Lower classification accuracy in low quality metaphases, which are difficult to classify manually
- Taking all metaphases into account still 88% of chromosomes were correctly assigned

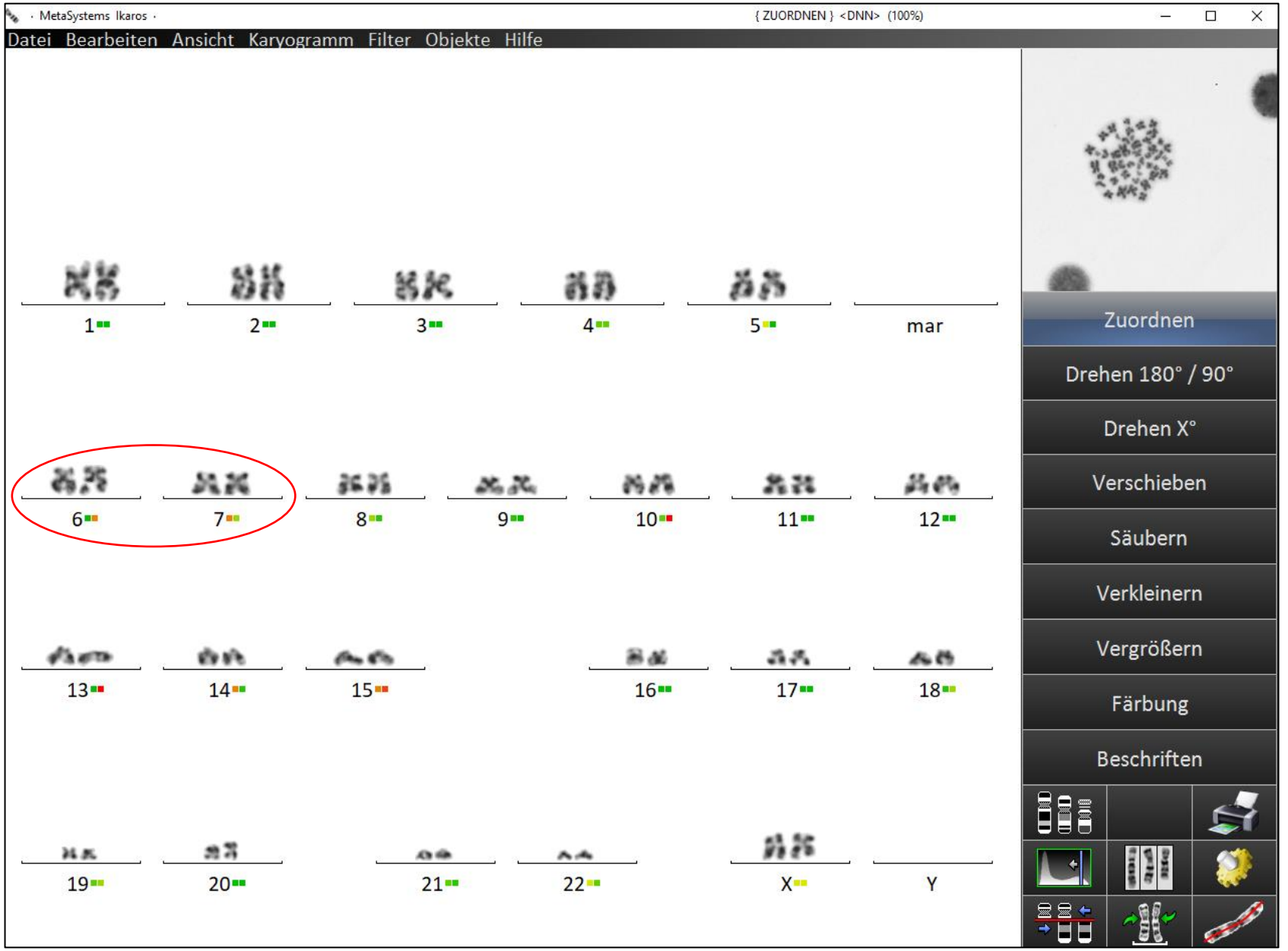
KI-basiertes Karyotypisieren

- automatisches Trennen der Chromosomen
- automatisches Legen des Karyogramms (NK)



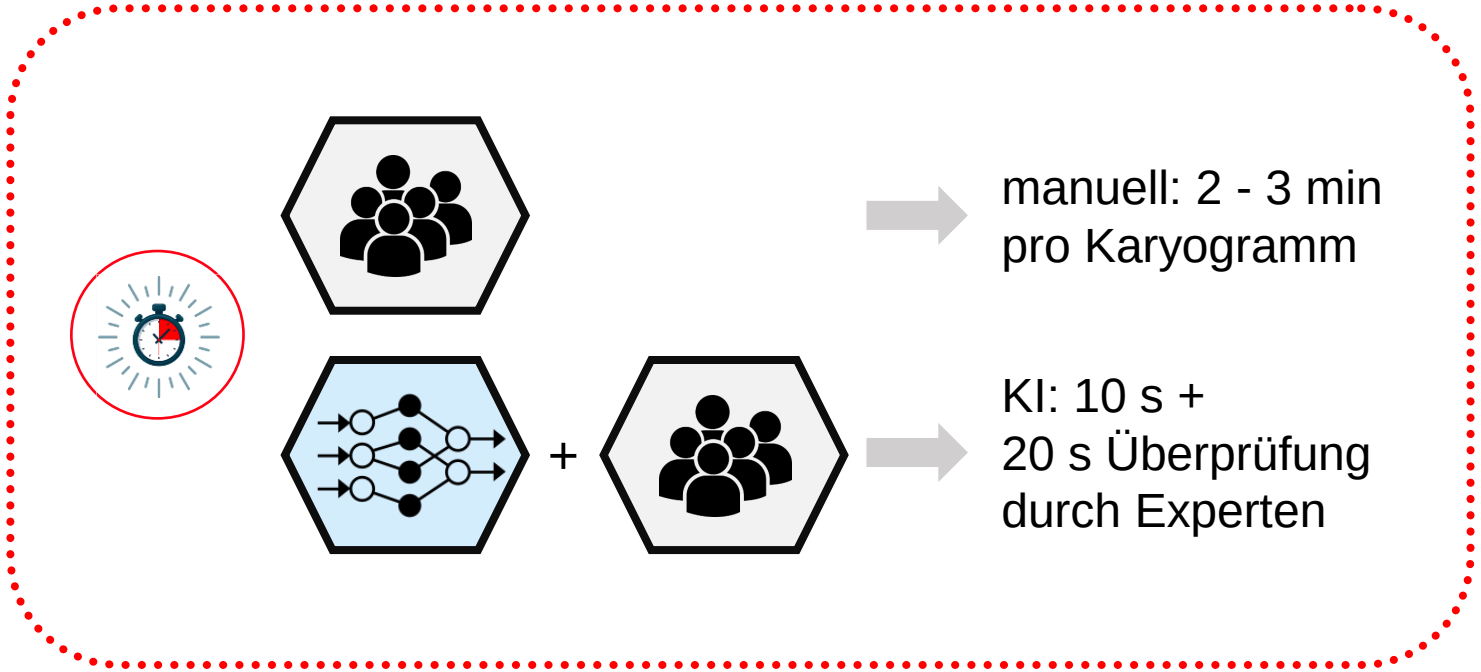
KI-basiertes Karyotypisieren:

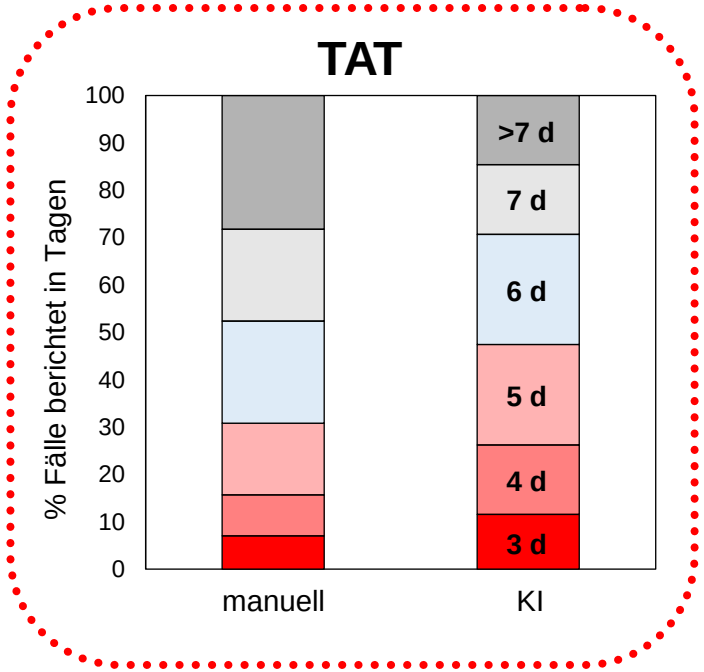
- Farbcode für Wahrscheinlichkeit der korrekten Zuordnung



KI-basierte Automatisierung der Chromosomenanalyse

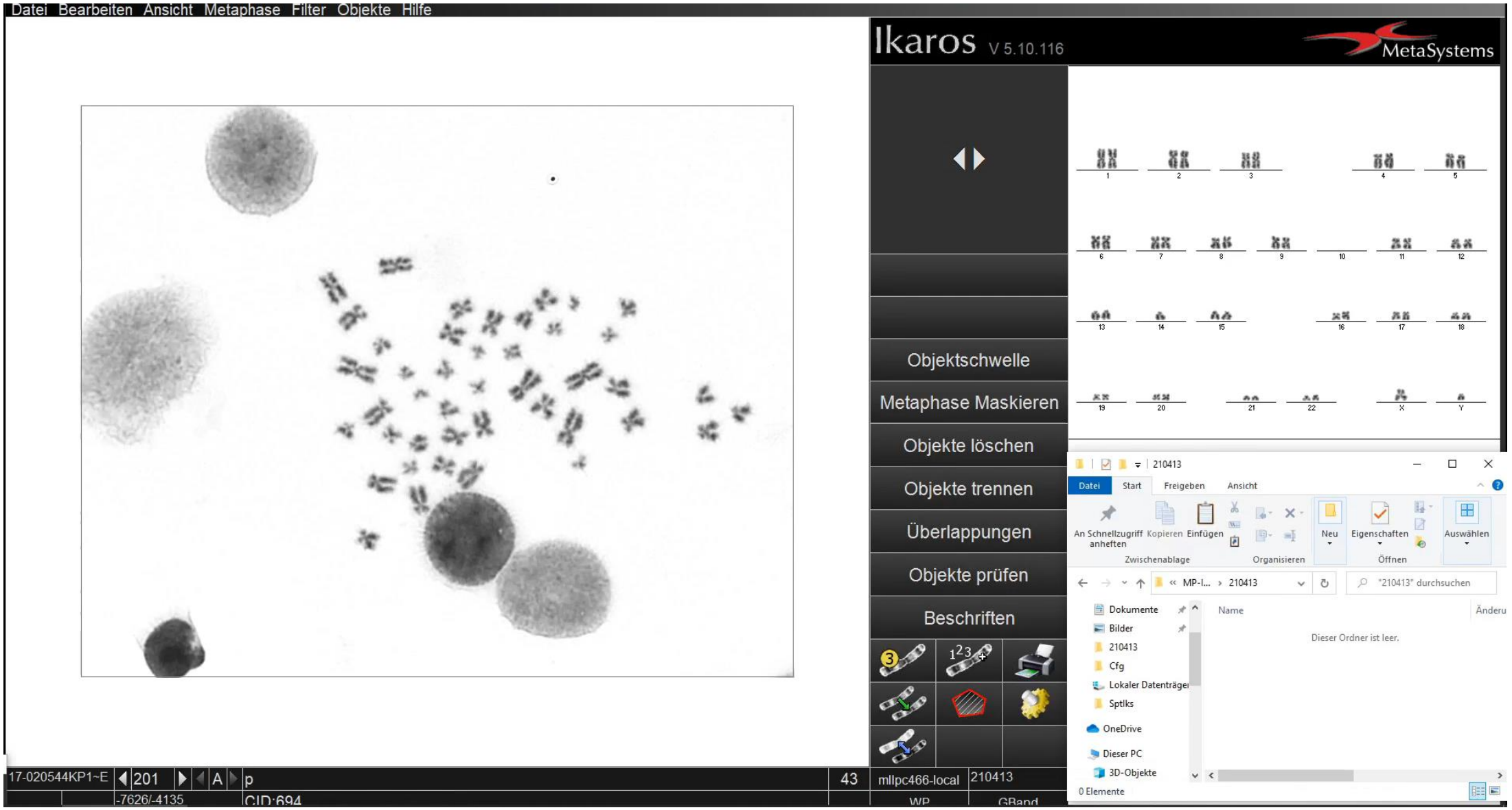
Einfluss auf Diagnostik





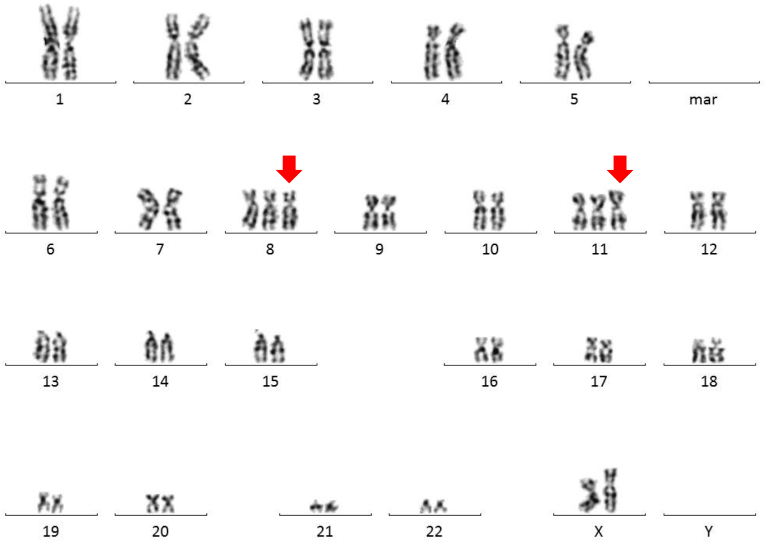
→ Reduktion der Turnaround-Zeit

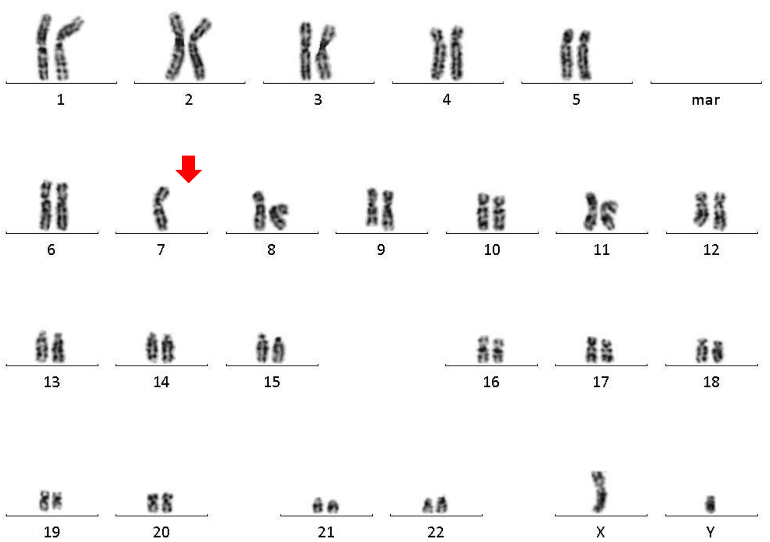
Batch-Karyotypisieren (20 MP)



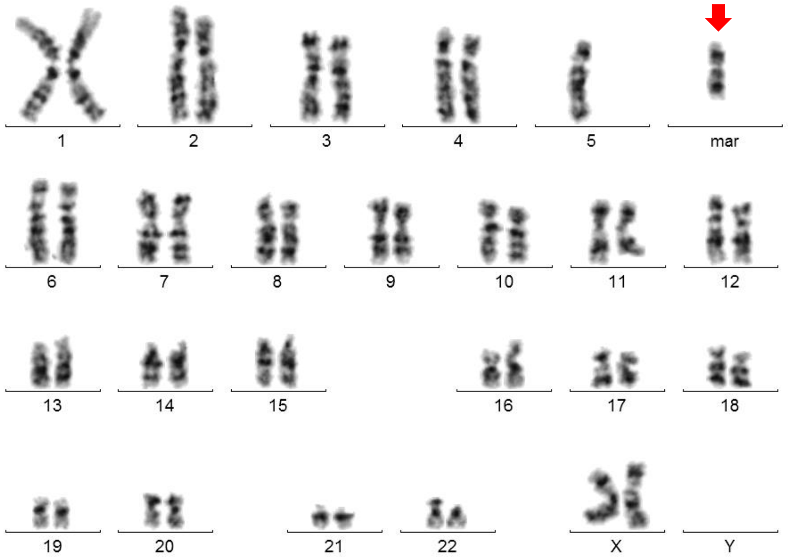
Automation of Karyotyping

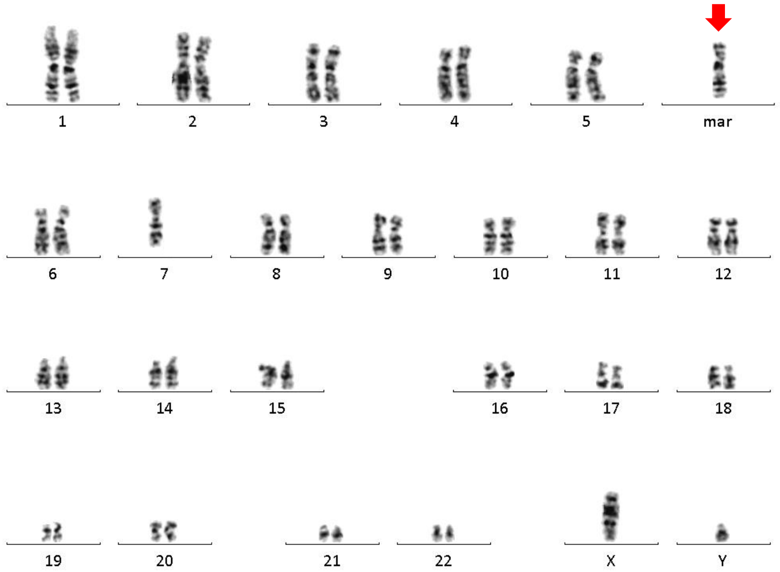
Classification of aberrant karyotype by AI-CN





Karyotypes with only numerical abnormalities are correctly classified as all chromosomes are structurally „normal“





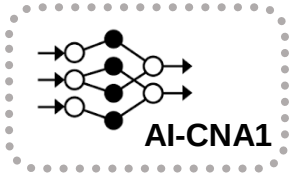
Derivative chromosomes clearly different from any normal chromosome left out for manual classification

AI-CN saves time

Automation of Karyotyping

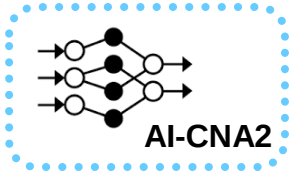
Next step: classification of abnormal chromosomes & detection of recurrent abnormalities

54,634 KG AK +
100,000 KG NK



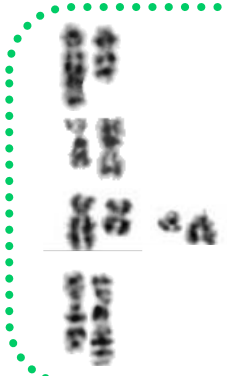
Lower false positive rate

54,634 KG AK +
54,634 KG NK



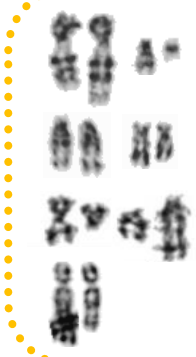
Higher detection rate

	n KG used for training	n cases used for validation	KG used for validation
t(9;22)(q34;q11)	12,766	34	600
del(5)(q14q34)	10,497	17	288
inv(16)(p13q22)	5,907	11	183
t(8;21)(q22;q22)	5,487	2	30
t(15;17)(q24;q21)	5,010	14	216
del(5)(q21q34)	4,163	11	148
inv(3)(q21q26)	3,838	5	64
t(9;11)(p21;q23)	2,744	2	30
der(1;7)(q10;p10)	2,377	3	37
t(11;14)(q13;q32)	1,845	7	59



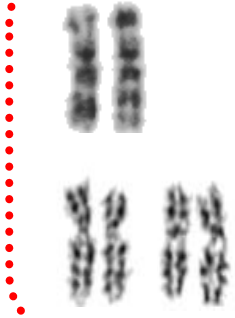
Abnormality detected as clonal in 100% of cases

Abnormality detected as clonal in 100% of cases



Abnormality detected as clonal in 80-99% of cases

Abnormality detected as clonal in 90-100% of cases



Abnormality detected as clonal in <80% of cases

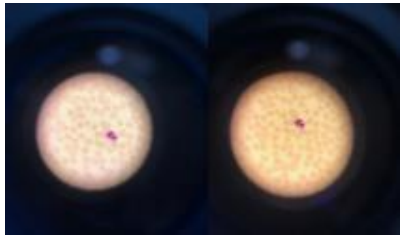
Abnormality detected as clonal in 100% of cases

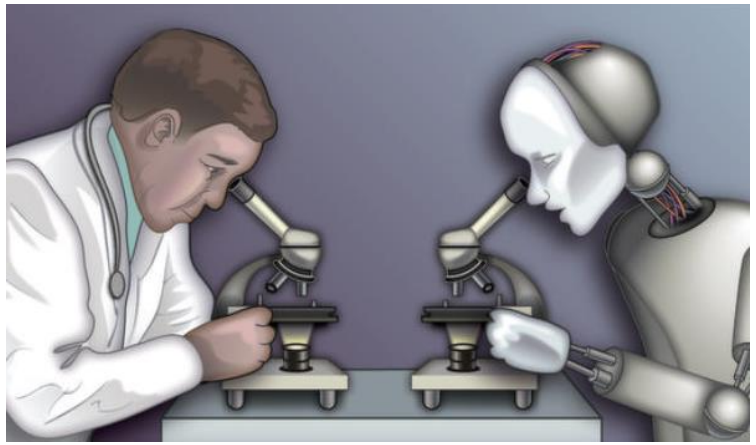
BELUGA Study („Better LeUkemia diaGnostics through AI“)

(Clinicaltrials.gov, NCT04466059) – classification of peripheral blood cells

29,119 patient samples (Jan 2021 – Jul 2022)

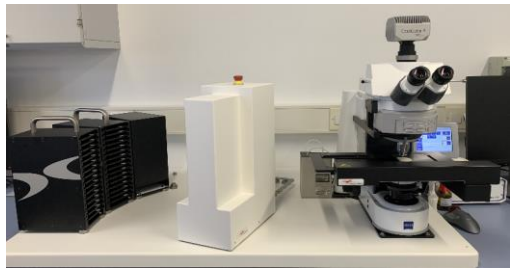
∑ = 2,911,915 cells differentiated

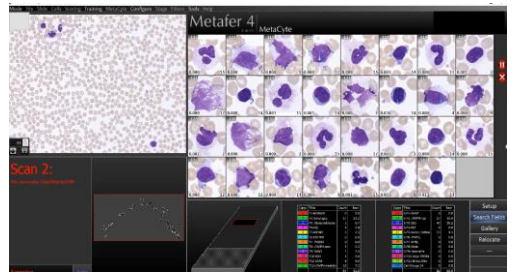




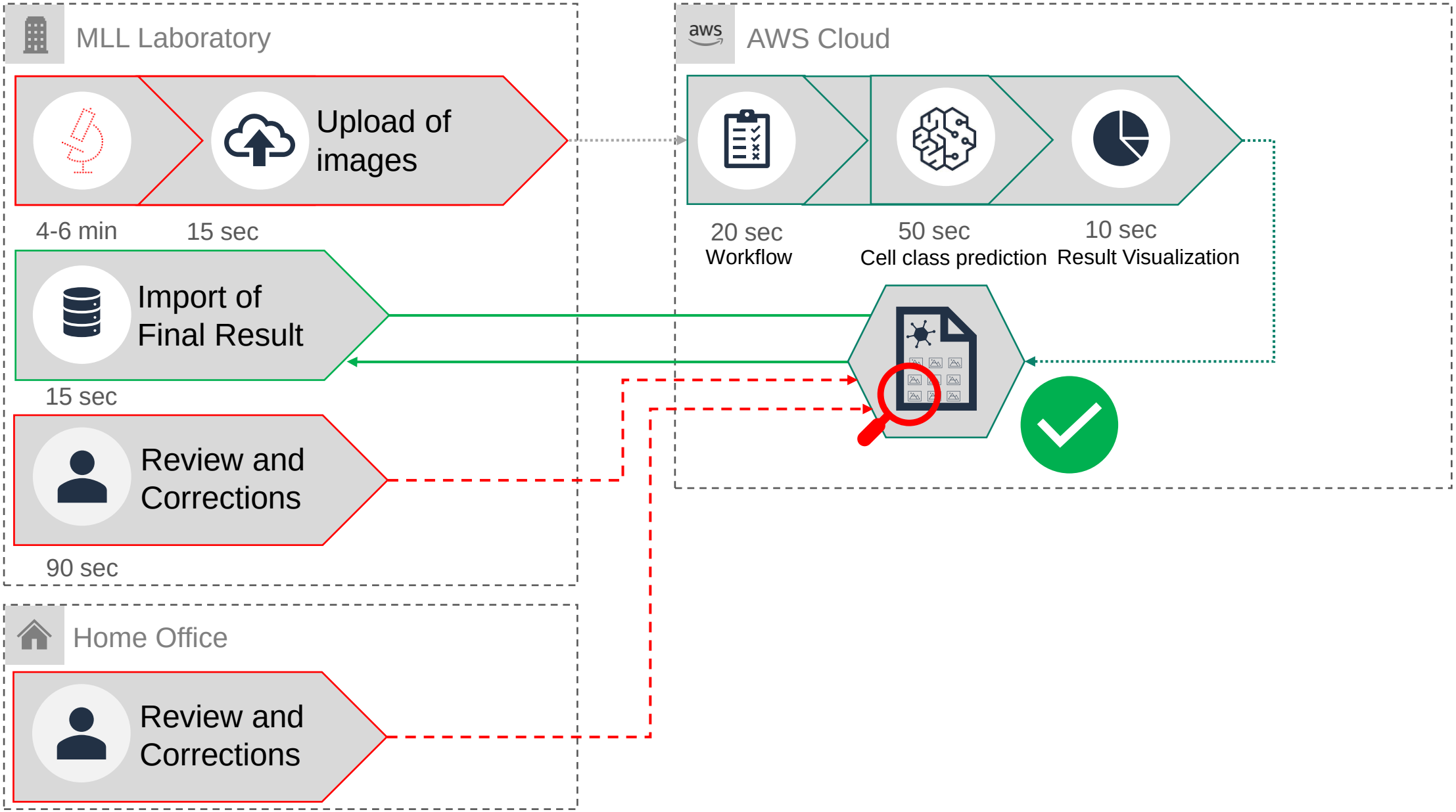
54%	Segmented Neutrophils	48%
1%	Bands	1,47%
2.3%	Concordance 94% for malignant/critical cells	2,69%
0.76%		2%
6.96%		7.05%
30.91%	Lymphocytes	24.53%
1.11%	Pathogenic blasts	3.25%

∑ = 14,322,972 cells differentiated

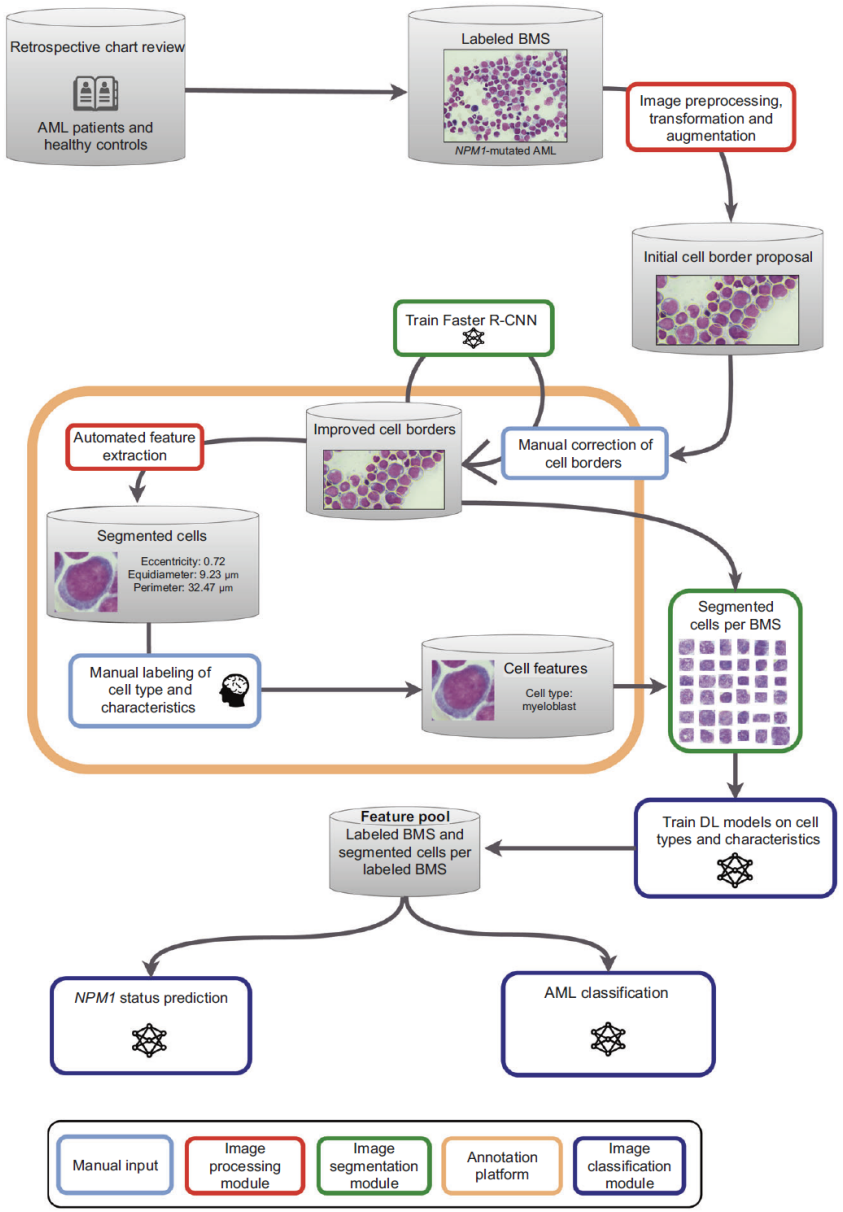




Integration of AI tool into routine diagnostics workflow



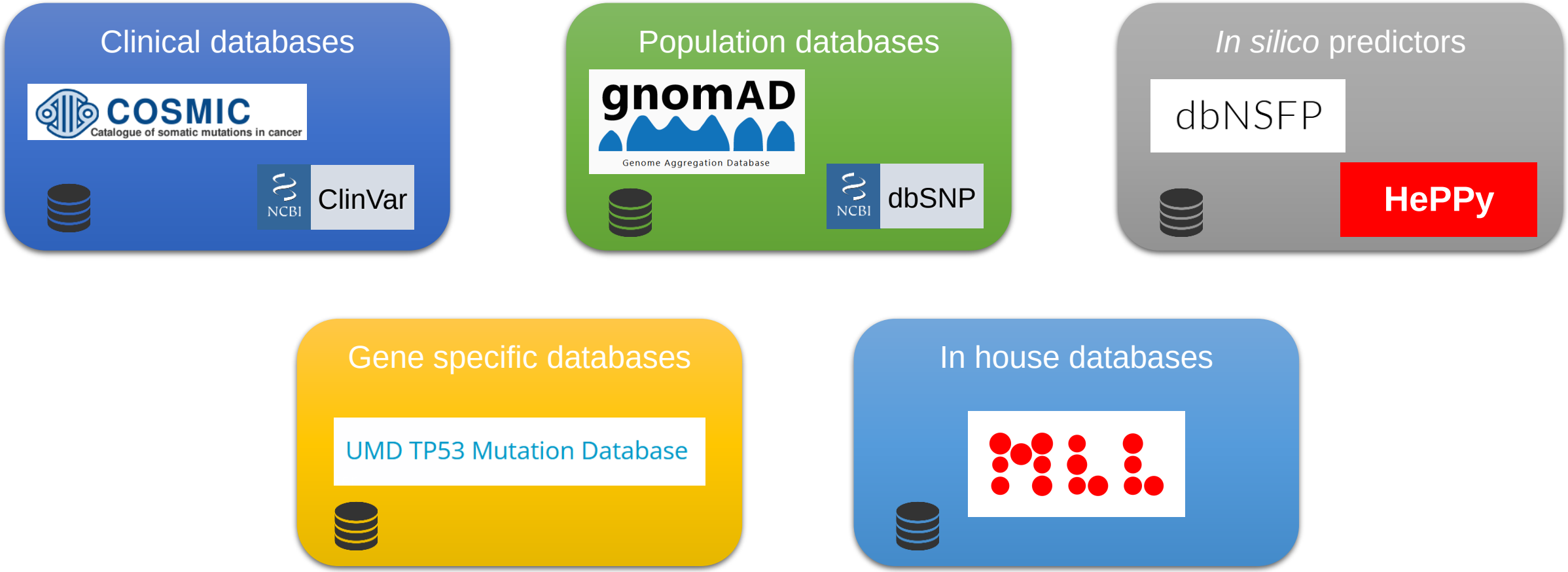
Einsatz von KI zur Prädiktion von AML und *NPM1* Mutationen



(A) AML vs. control	Prediction by deep learning	
	Healthy control	AML
Ground truth		
Healthy control	43 (89%)	5 (11%)
AML	28 (13%)	223 (87%)
(B) mNPM1 vs. wtNPM1	**Prediction by deep learning**	
	wt*NPM1*	**m*NPM1***
Ground truth		
wt*NPM1*	149 (86%)	24 (14%)
m*NPM1*	11 (14%)	66 (86%)

J.-N. Eckardt et al., Leukemia 2022 36:111–118

NGS: Interpretation von Varianten



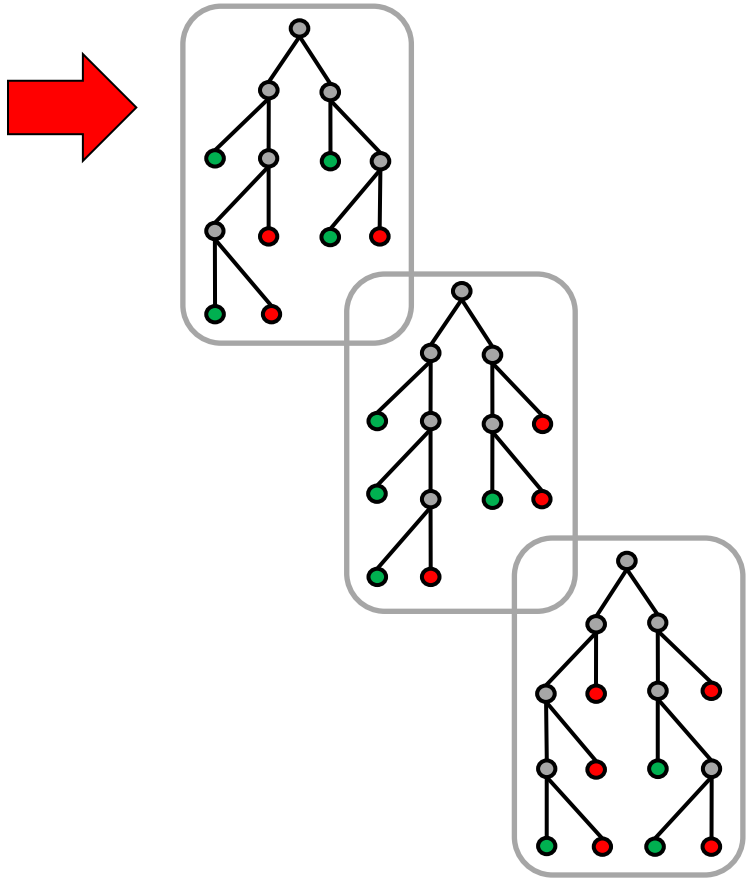
Herausforderung: finale Interpretation der Informationen aus den diversen Quellen

HePPy: A hematological (meta) predictor of pathogenicity

~500 manuell kuratierte Varianten mit eindeutiger Zuordnung als “somatische Mutation” oder “benigner Polymorphismus”

Predictor
PROVEAN
VEST3
M-CAP
SIFT
Polyphen-2
FATHMM
FATHMM-MKL
Mutation Assessor
LRT
Mutation Taster

Random forest model



HePPy-Score	0.997

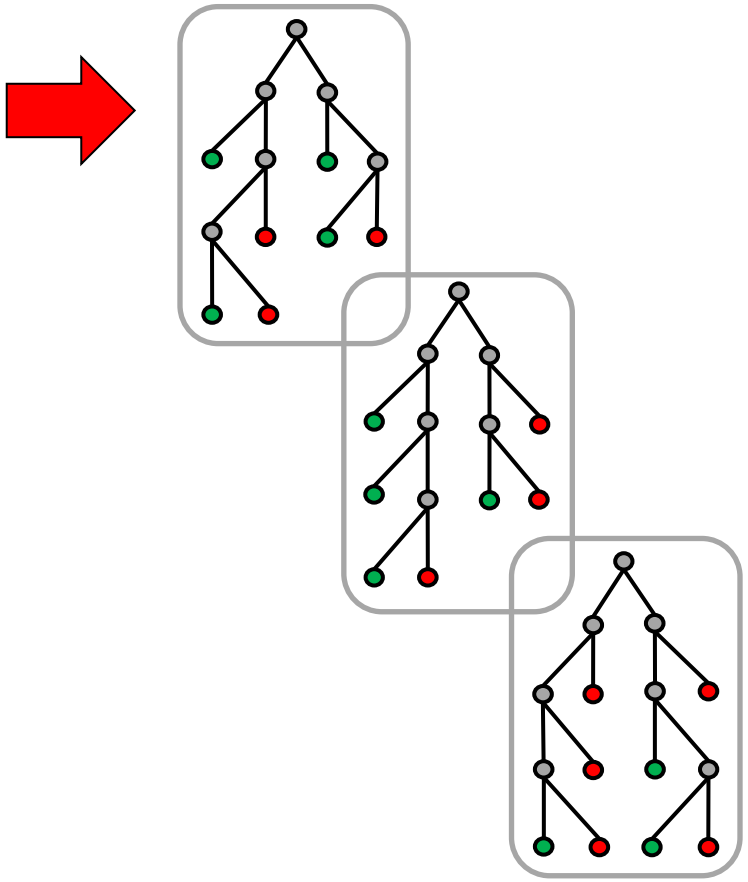
HePPy: A hematological (meta) predictor of pathogenicity – ein Beispiel

TP53: c.1027G>C

A variant with conflicting *in silico* predictions

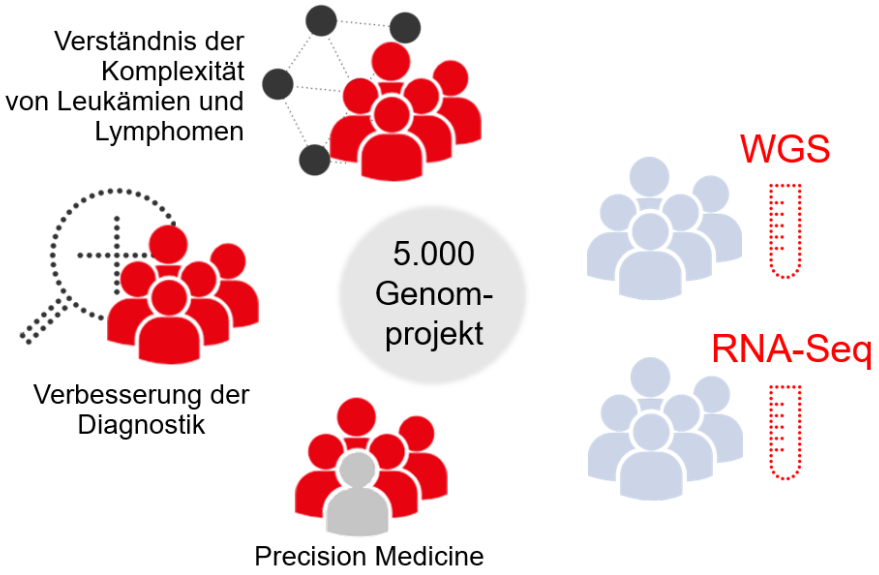
Predictor	Score
PROVEAN	-0.26
VEST3	0.175
M-CAP	0.047
SIFT	0.045
Polyphen-2	0.238
FATHMM	-3.23
FATHMM-MKL	0.815
Mutation Assessor	2.05
LRT	0.023
Mutation Taster	1.0

Random forest model

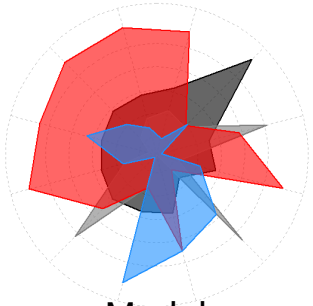


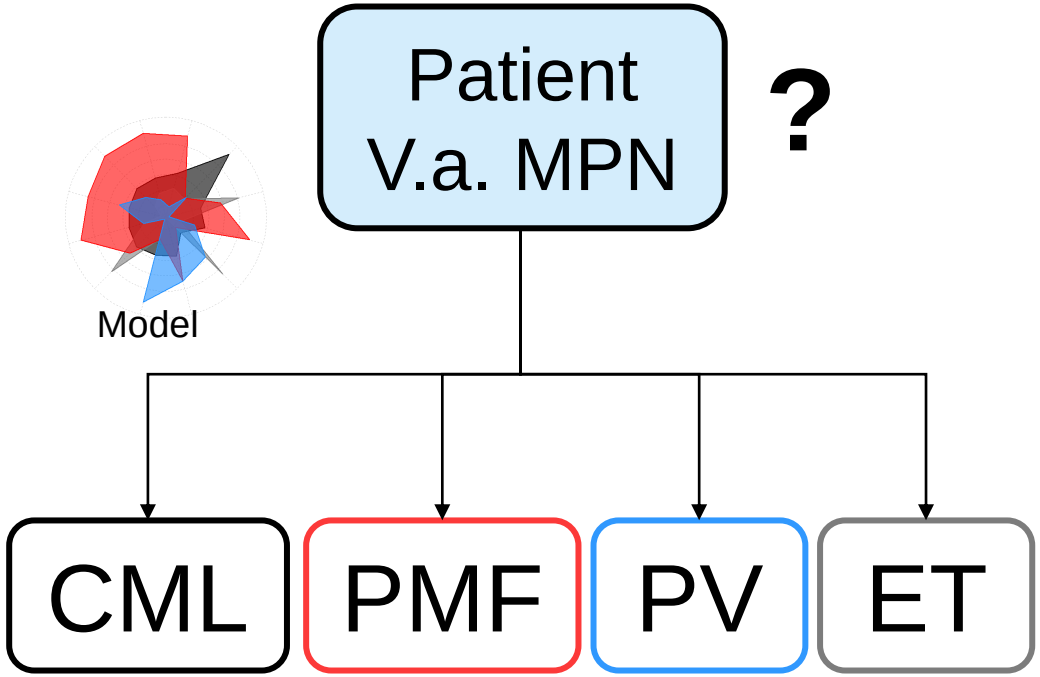
HePPy	0.066

Klassifizierung von MPN anhand des Mutationsprofils

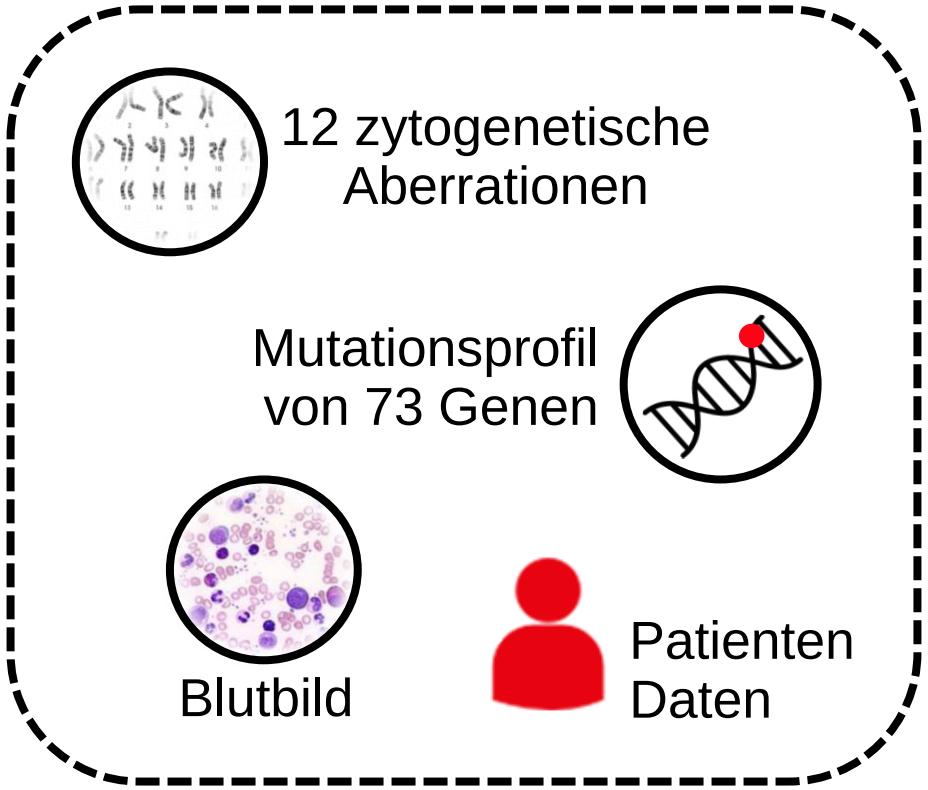


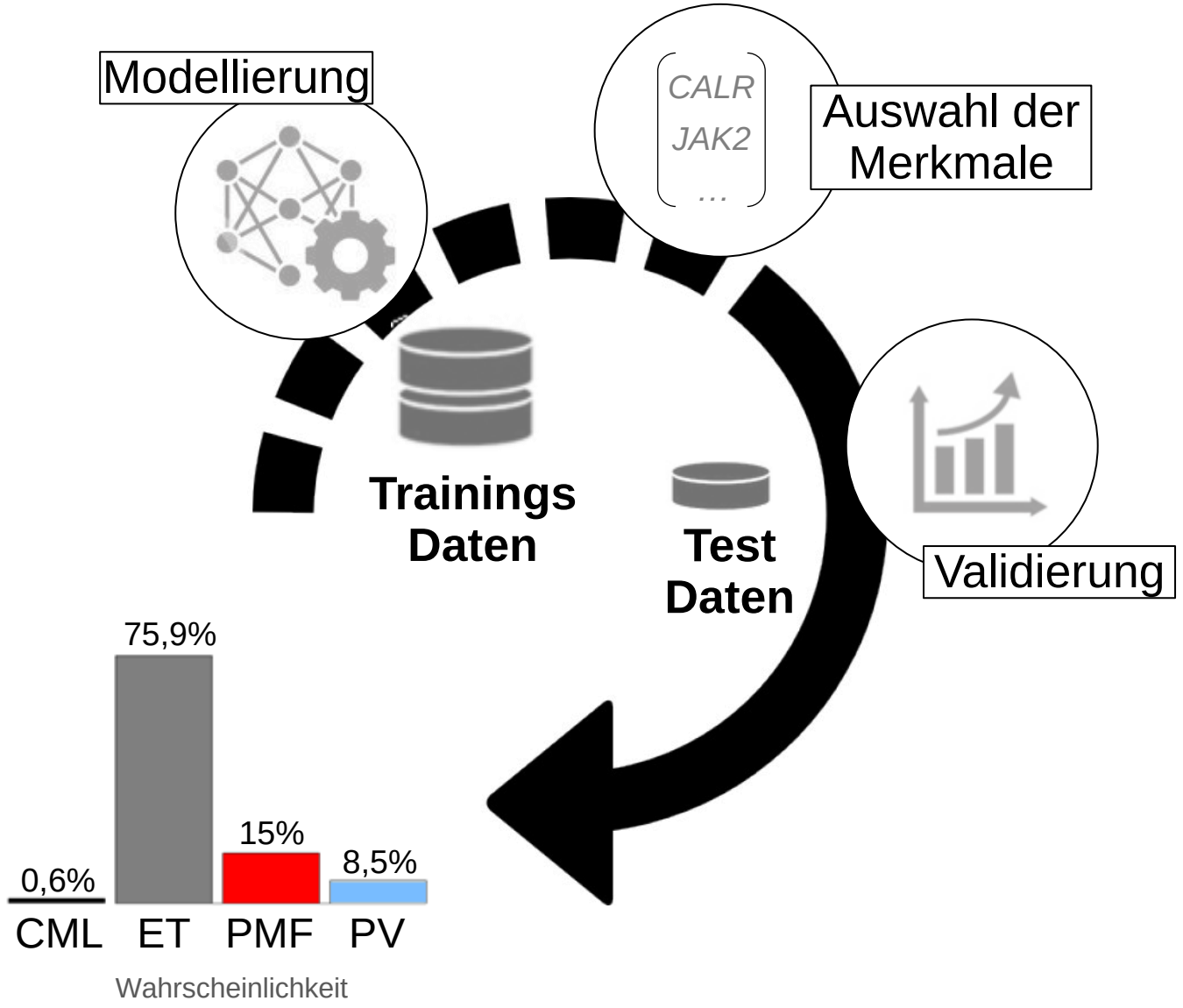
Training eines Algorithmus





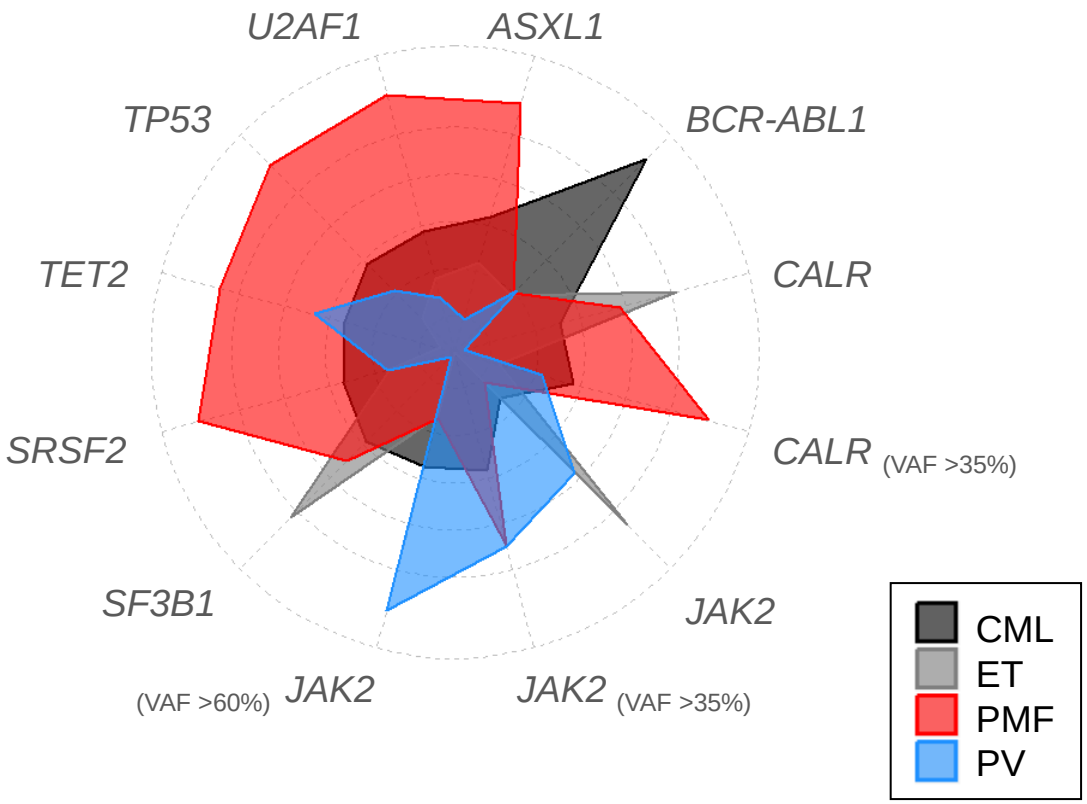
Klassifizierung von MPN anhand des Mutationsprofils





Klassifizierung von MPN anhand des Mutationsprofils

Finales Model

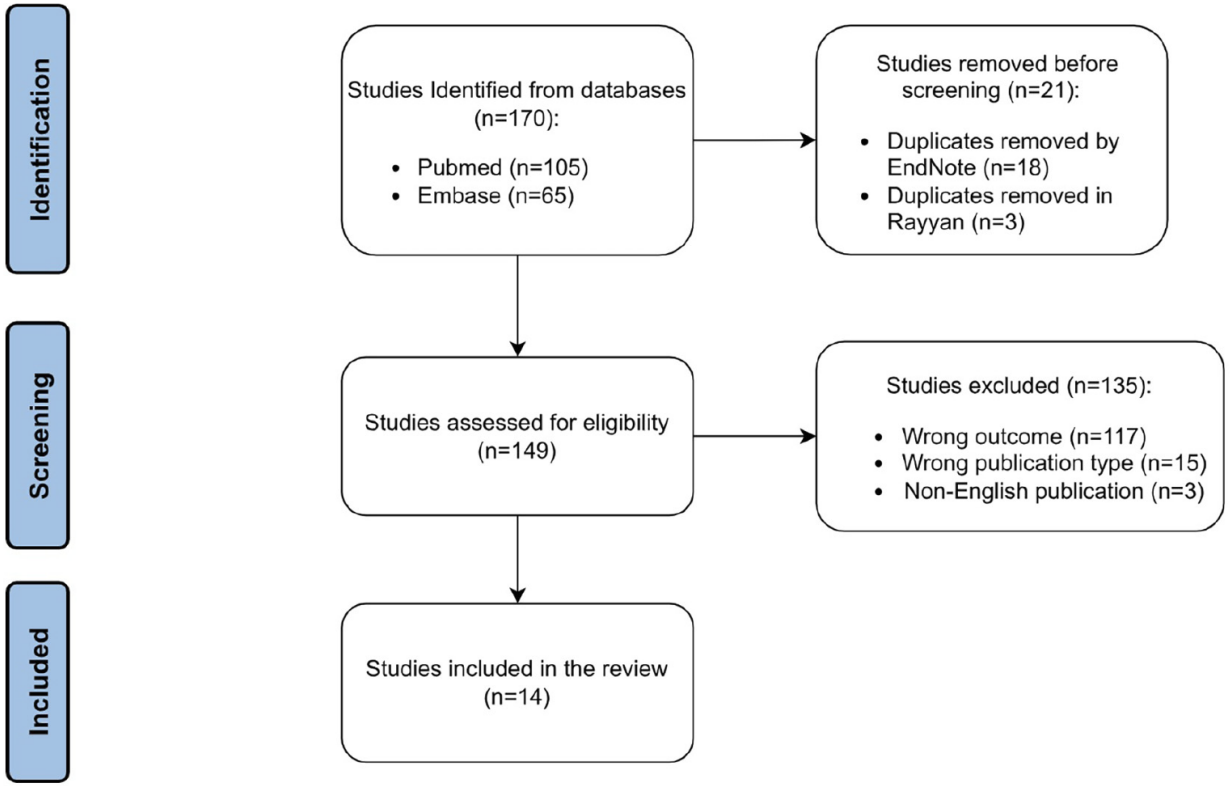


Morphologie

Algorithmus	CML	ET	PMF	PV
CML	48	0	0	0
ET	0	53	0	1
PMF	0	1	34	0
PV	0	1	0	39

Accuracy: 98,3%

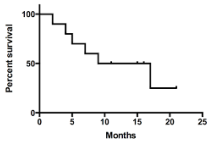
Publikationen zur Diagnose und Klassifikation der CLL mit KI-Methoden



Reference	Outcome	Advantages	Disadvantages
Zhang, Qureshi et al. (2023)	Diagnosis and classification of tumors using targeted RNA expression profiling	- Lower chance of overfitting - Can give information about cancer biology, prognosis, and therapeutic targets	- NGS is not routinely ordered for CLL workup - Data did not include mutations and chromosomal abnormalities - The model was not externally validated
Zhu, Gan et al. (2022)	Identification of diagnostic biomarkers for CLL using GEO database	- Combination of bioinformatic analyses and ML - Validation of the identified genes	- High risk of batch effects due to usage of multiple datasets from the GEO database
Xia, Leon et al. (2021)	Diagnosis and classification of SBCLs using DNA methylation profiling	- Able to classify CLL/SLL, MCL, MZL, FL with high accuracy - The model is available online for research use - The model was internally and externally validated	- Unsupervised analysis was not possible due to significant batch effects
Abhishek, Jha et al. (2023)	Diagnosis and classification of leukemia using images of blood smears	- Able to classify ALL, AML, CLL, CML, and normal samples - Uses only images of peripheral blood smear - CNN models were used as feature extractors to optimize the performance of the classifier - The models were internally and externally validated	- Time taken for classification was not mentioned - The entire sample of CLL images was obtained from 7 patients only - Dataset used to train feature extractors was different from the one used to train the classifier (negative transfer)
Dese, Raj et al. (2021)	Diagnosis and classification of leukemia using images of blood smears	- Able to classify ALL, AML, CLL, CML, and normal samples - Uses only images of peripheral blood smear - Rapid time to diagnosis (<1 min) - ML algorithms used in feature extraction to optimize performance of the classifier	- The model was not externally validated
Mohammed, Mohamed et al. (2017)	Diagnosis of CLL using images of blood smears	- SVM was used for lymphocyte segmentation - Multiple ML models were evaluated for the classification task - majority voting fusion method was used to improve classification performance - Can be used as a quick and cheap screening tool for CLL	- The image acquisition method used in the study differs from other clinical settings - A search technique for cells is needed to obtain images similar to the ones in the study
Simonson, Lee et al. (2022)	Predict whether additional antibody panel should be ordered to distinguish CLL from MCL	- Use of ensemble learning - Models utilize flow cytometry data - Models were evaluated prospectively on new cases - Models were internally and externally validated	- Dataset lacked information on previous diagnoses of leukemia/lymphoma - The model was developed using data from a single laboratory
Ng and Zuromski (2021)	Diagnosis and classification of B-cell malignancies using flow cytometry	- Able to classify BNHL, B-ALL/LBL, CLL, DLBCL, and others accurately - Able to detect BNHL and B-ALL/LBL cases that require confirmatory studies - Relatively large sample - Rapid time to diagnosis (−35 s) - Use of UMAP for dimensionality reduction	- Difficulty of troubleshooting the misclassifications
Zhao, Mallesh et al. (2020)	Diagnosis and classification mature B-cell neoplasms using flow cytometry	- Able to classify seven subtypes of mature B-cell neoplasms (CLL, MCL, PL, LPL, MZL, FL, HCL), MBL, and normal samples - Large sample - Use of SOM for dimensionality reduction	- Specific performance metrics for CLL classification were not reported - Time taken for classification was not mentioned
Haider, Ujjan et al. (2022)	Early diagnosis and classification of leukemia using CBC	- Able to classify ALL, AML, APML, CLL, CML, and others - Able to accurately detect and subtype leukemia using only CBC items and CPD	- The model was not externally validated - Time taken for classification was not mentioned
Steinbuss, Kriegsmann et al. (2021)	Diagnosis and classification of NHL using LNs histopathological images	- Relatively large sample - Use of quality control limits to improve accuracy	- The model can only classify two disease entities - Low sensitivity in detecting CLL/SLL
do Nascimento, Martins et al. (2018)	Diagnosis and classification of NHL using LNs histopathological images	- Able to classify CLL, MCL, and FL - Multiple classifiers were evaluated in the study - Multiple statistical methods were applied to optimize feature selection	- Small sample - The model was not externally validated - The proposed algorithm requires long processing time
Zhang, Cui et al. (2020)	Classification of NHL subtypes using histopathological images	- Able to classify CLL, FL, and MCL - TL and PCA were used for fine-tuning and feature extraction, with a neural network model used for classification	- The model was not externally validated - Time taken for classification was not mentioned
Féré, Gobinet et al. (2020)	Diagnosis of CLL using Raman data	- The use of rdCV to reduce overfitting - The use of adaptive decision thresholds to adapt the model to different clinical scenarios - The use of consensus label strategy to improve model stability - The use of four tests to ensure the quality of Raman data - Rapid time to diagnosis (13 s) - Can be used to study biochemical changes in CLL	- Raman spectroscopy is not routinely ordered for CLL workup

M. Elhadary et al., Blood Reviews 2023; doi: 10.1016/j.blre.2023.101134. Online ahead of print

Risikostratifizierung AML – Standard versus KI



Standard: basierend auf Hypothesen und Literaturdaten

Table 5. 2017 ELN risk stratification by genetics

Risk category*	Genetic abnormality
Favorable	t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*
	inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*
	Mutated *NPM1* without *FLT3*-ITD or with *FLT3*-ITD^{low}†
	Biallelic mutated *CEBPA*
Intermediate	Mutated *NPM1* and *FLT3*-ITD^{high}†
	Wild-type *NPM1* without *FLT3*-ITD or with *FLT3*-ITD^{low}† (without adverse-risk genetic lesions)
	t(9;11)(p21.3;q23.3); *MLLT3-KMT2A*‡
	Cytogenetic abnormalities not classified as favorable or adverse
Adverse	t(6;9)(p23;q34.1); *DEK-NUP214*
	t(v;11q23.3); *KMT2A* rearranged
	t(9;22)(q34.1;q11.2); *BCR-ABL1*
	inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2,MECOM(EVI1)*
	−5 or del(5q); −7; −17/abn(17p)
	Complex karyotype,§ monosomal karyotype‖
	Wild-type *NPM1* and *FLT3*-ITD^{high}†
	Mutated *RUNX1*¶
	Mutated *ASXL1*¶
	Mutated *TP53*#

H. Döhner et al., Blood. 2017; 129(4):424-447

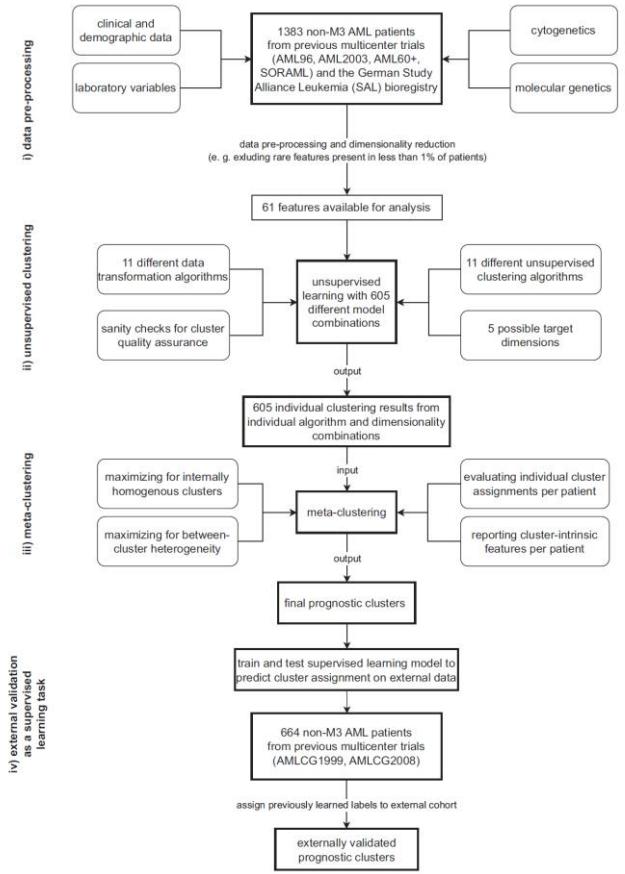
KI: basierend auf „unsupervised and supervised learning“

Start mit Rohdaten
Extraktion von relevanten Variablen

Unsupervised clustering

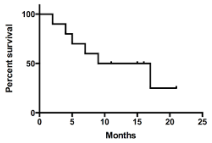
Meta-Clustering
Finale Cluster

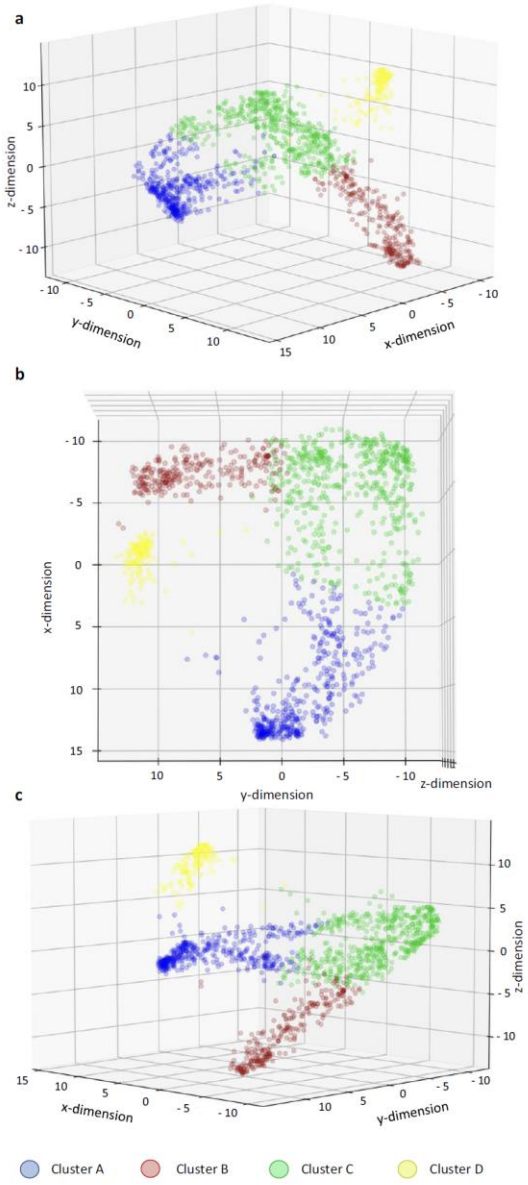
Externe Validierung

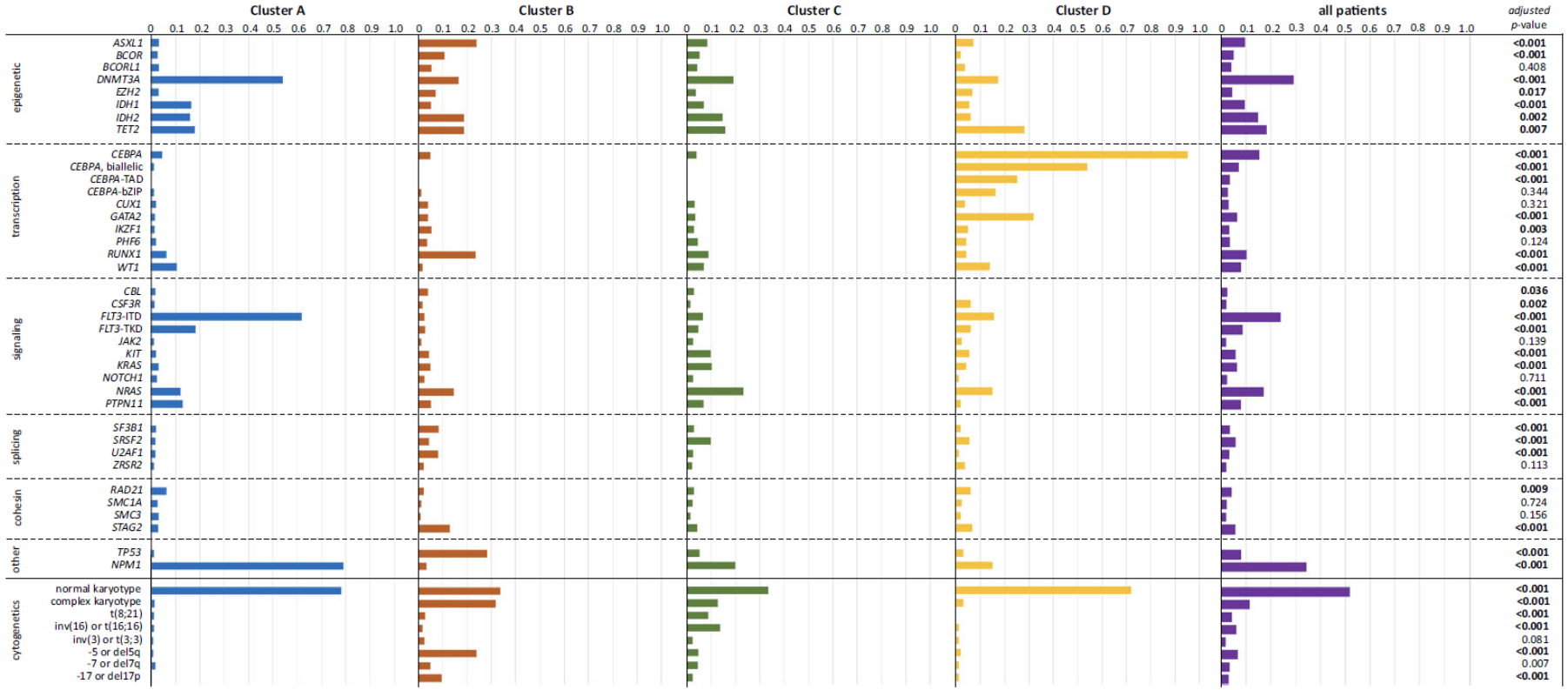


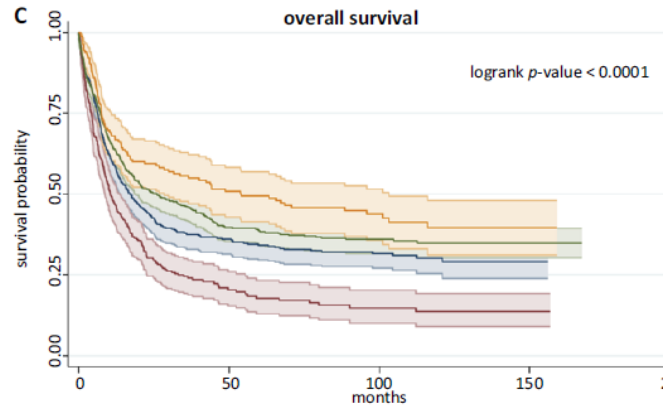
J.-N. Eckardt et al., Commun Med 2023;3:68

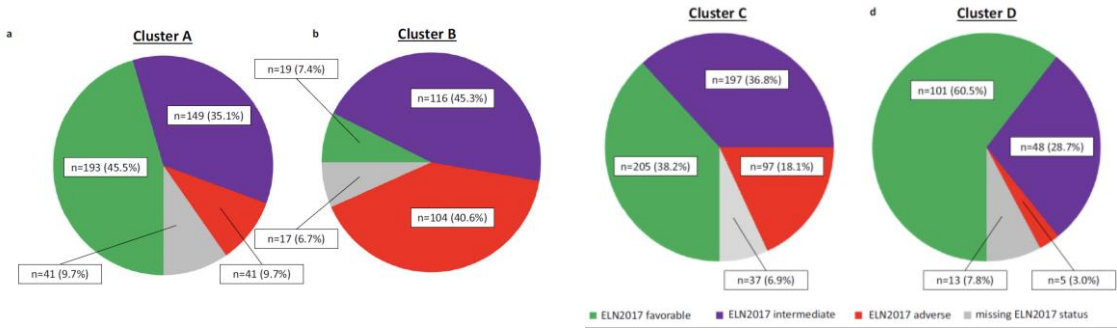
Risikostratifizierung AML basierend auf KI





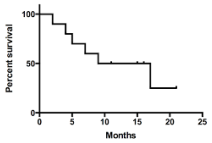




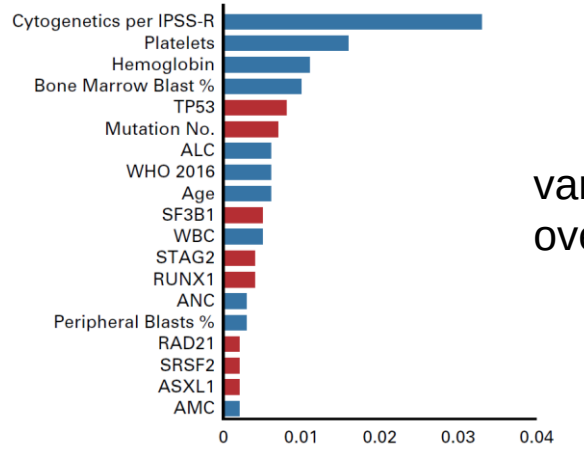


J.-N. Eckardt et al., Commun Med 2023;3:68

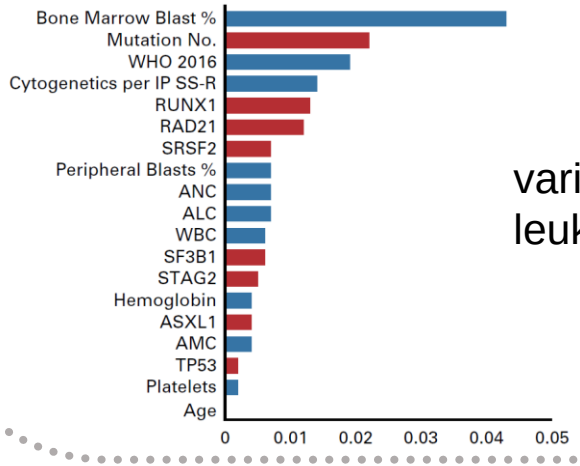
Risikostratifizierung MDS – KI versus IPSS-R



AI-model was built based on clinical and mutational data entered into random survival forest algorithm

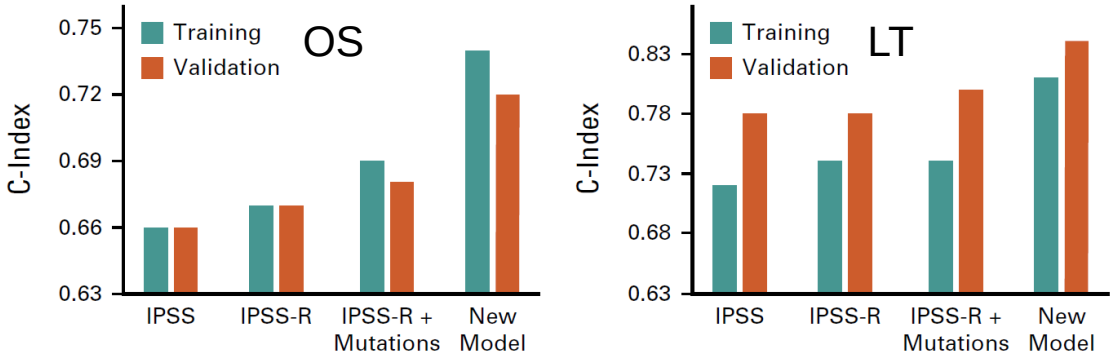


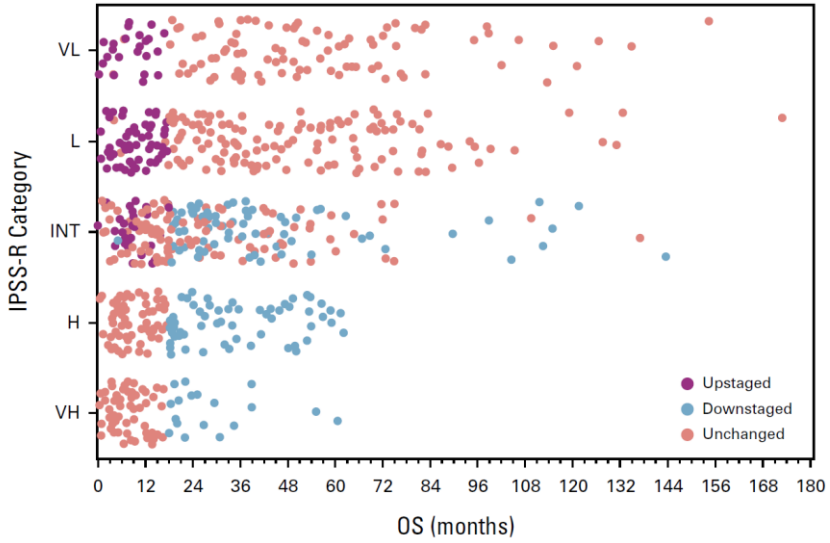
variable importance for overall survival



variable importance for leukemia transformation

Comparison to IPSS-R





A. Nazha et al., JCO 2021; 39(33):3737-3746

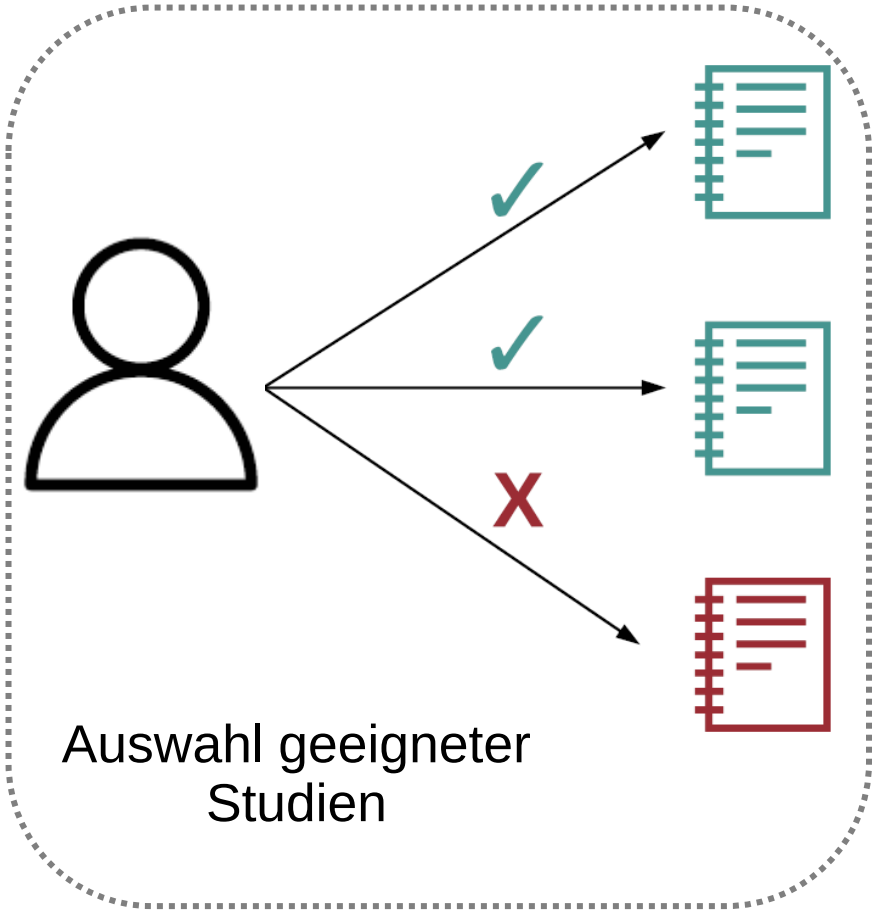
Therapie-Planung und Individualisierung der Therapie

Patienten-zentrierte Auswahl klinischer Studien

Clinical trials.gov

Extraktion für Studieneinschluss relevanter Parameter

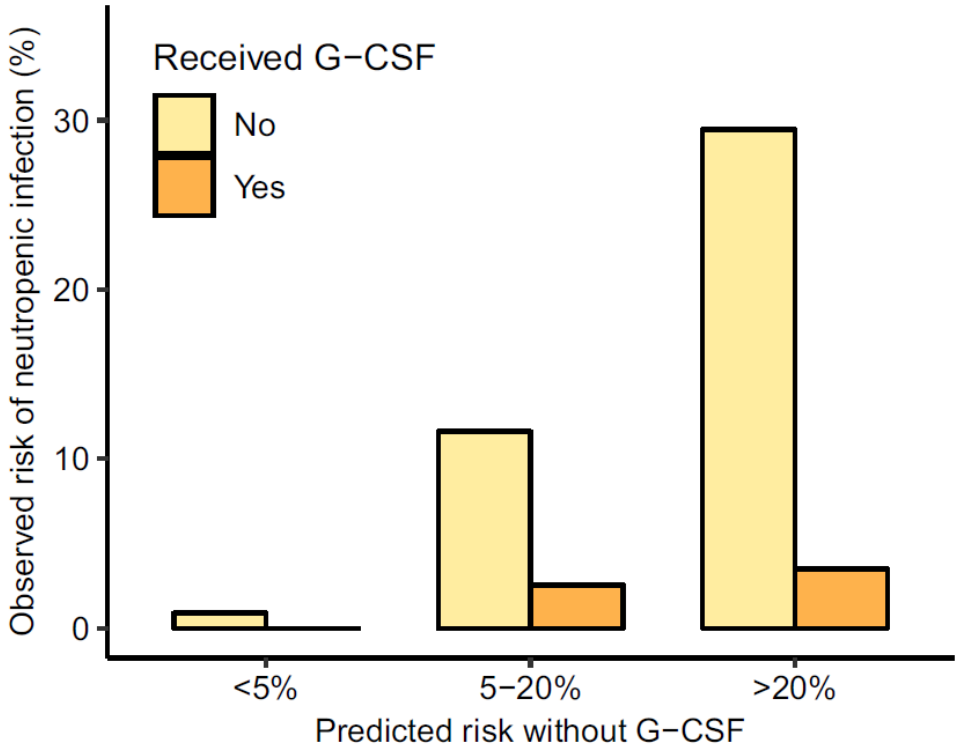
Automatischer Abgleich mit Patientendaten



S. Kaskovich et al., JCO CCI 2023

Therapie Monitoring und Früherkennung unerwünschter Ereignisse

Risiko-Prädiktion Chemotherapie induzierter Neutropenie und Infektion



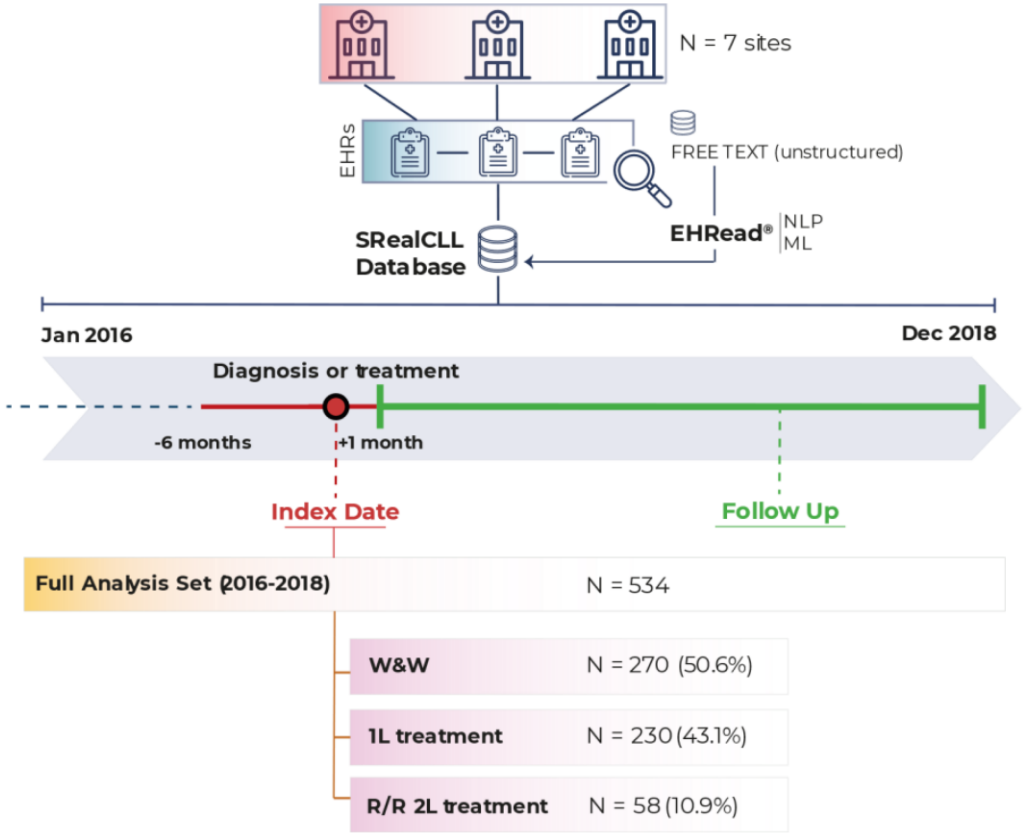
M. S. Venäläinen et al., Cancer Medicine 2022;11:654–663

Model zur Risikoeinschätzung von Chemotherapie-induzierter Myelosuppression bei Kindern mit Wilmstumor

Ergebnis individueller Risikoscore mit Angabe von Risikofaktoren und protektiven Faktoren basierend 19 Variablen extrahiert aus 40 primär evaluierten Variablen

M. Li et al., Cancer 2023; 5:1078

Unterstützung bei klinischen Entscheidungen durch Aufbereitung von Daten



Comorbidity	W&W n = 270	1L Treatment n = 230	R/R 2L Treatment n = 58
Cardiovascular, n (%)	117 (43.3)	111 (48.3)	30 (51.7)
Hypertension	96 (35.6)	88 (38.3)	23 (39.7)
Cardiac arrhythmia	45 (16.7)	41 (17.8)	10 (17.2)
Atrial fibrillation	24 (8.9)	19 (8.3)	4 (6.9)
Atrial flutter	5 (1.9)	4 (1.7)	2 (3.4)
Heart failure	44 (16.3)	40 (17.4)	10 (17.2)
Ischemic heart disease	28 (10.4)	22 (9.6)	6 (10.3)
Heart valve disorder	18 (6.7)	20 (8.7)	6 (10.3)
Gastrointestinal and hepatobiliary, n (%) †	105 (38.9)	89 (38.7)	17 (29.3)
Hepatomegaly	16 (5.9)	25 (10.9)	6 (10.3)
Hepatitis C	6 (2.2)	4 (1.7)	1 (1.7)
Peptic ulcer	7 (2.6)	4 (1.7)	2 (3.4)
Hiatal hernia	7 (2.6)	9 (3.9)	1 (1.7)
Endocrine, metabolism, and nutrition, n (%)	82 (30.4)	70 (30.4)	23 (39.7)
Diabetes mellitus	66 (24.4)	56 (24.3)	18 (31.0)
Dyslipidemia ‡	37 (13.7)	43 (18.7)	11 (19.0)
Musculoskeletal and connective tissue, n (%)	81 (30.0)	70 (30.4)	22 (37.9)
Rheumatoid arthritis	19 (7.0)	19 (8.3)	4 (6.9)
Osteoarthritis	8 (3.0)	4 (1.7)	2 (3.4)
Renal and urinary system, n (%)	42 (15.6)	33 (14.3)	7 (12.1)
Chronic renal failure	29 (10.7)	22 (9.6)	5 (8.6)
Diabetic nephropathy	4 (1.5)	0 (0)	0 (0)
Nephrolithiasis	5 (1.9)	1 (0.4)	0 (0)
Urinary tract infectious disease	15 (5.6)	14 (6.1)	3 (5.2)
Respiratory, n (%)	26 (9.6)	28 (12.2)	3 (5.2)
COPD	15 (5.6)	18 (7.8)	0 (0)
Bronchial asthma	14 (5.2)	12 (5.2)	3 (5.2)
Pulmonary hypertension	4 (1.5)	4 (1.7)	0 (0)

Antineoplastic Treatments	1L Treatment n = 230	R/R 2L Treatment n = 58
Ibrutinib, n (%)	149 (64.8)	36 (62.1)
Bendamustine + rituximab, n (%)	29 (12.6)	2 (3.5)
Obinutuzumab + chlorambucil, n (%)	12 (5.2)	3 (5.2)
Chlorambucil + rituximab, n (%)	11 (4.8)	1 (1.7)
Idelalisib + rituximab, n (%)	9 (3.9)	4 (6.9)
Fludarabine + cyclophosphamide + rituximab, n (%)	8 (3.5)	1 (1.7)
Ibrutinib + obinutuzumab, n (%)	6 (2.6)	-
Venetoclax, n (%)	5 (2.2)	9 (15.5)
Venetoclax + rituximab, n (%)	1 (0.4)	2 (3.5)

Concomitant Medication	W&W n = 270	1L Treatment n = 230	R/R 2L Treatment n = 58
Antihypertensive and/or antiarrhythmic drugs, n (%)	80 (29.6)	103 (44.8)	18 (31.0)
Antithrombotic drugs, n (%)	79 (29.3)	98 (42.6)	16 (27.6)
Diuretic drugs, n (%)	38 (14.1)	75 (32.6)	20 (34.5)
Lipid-lowering drugs, n (%)	37 (13.7)	69 (30.0)	12 (20.7)
Cardiotonic drugs, n (%)	13 (4.8)	6 (2.6)	2 (3.4)
Antianginal/vasodilator drugs, n (%)	8 (3.0)	19 (8.3)	5 (8.6)
Peripheral vasodilator drugs, n (%)	1 (0.4)	2 (0.9)	0 (0)

J. Loscertales et al., Cancers 2023

Was notwendig ist, um KI erfolgreich einzusetzen

- Verfügbarkeit von gut annotierten Datensätzen von hoher Qualität und in ausreichender Menge
- Gute Datenqualität und – standarisierung erforderlich für zuverlässige KI-Vorhersagen (fehlende, unvollständige, widersprüchliche und fehlerhafte Daten müssen bearbeitet werden)
- Infrastruktur und Rechenressourcen zur Verarbeitung und Analyse großer Datenmengen
- Zusammenarbeit und interdisziplinäres Fachwissen zwischen medizinischen Fachkräften, Datenwissenschaftlern, KI-Experten und Regulierungsbehörden
- kontinuierliche Überwachung und Verbesserung, um auf dem neuesten Stand zu bleiben, genau zu sein und den sich entwickelnden klinischen Anforderungen gerecht zu werden
- Einhaltung ethischer und gesetzlicher Vorschriften
- Validierung und behördliche Zulassung zum Nachweis der Sicherheit, Wirksamkeit und Zuverlässigkeit in der klinischen Praxis, Schulung und Ausbildung der Nutzer, um die Fähigkeiten und Grenzen von KI-Systemen zu verstehen

Lessons learned from translating AI from development to deployment in healthcare

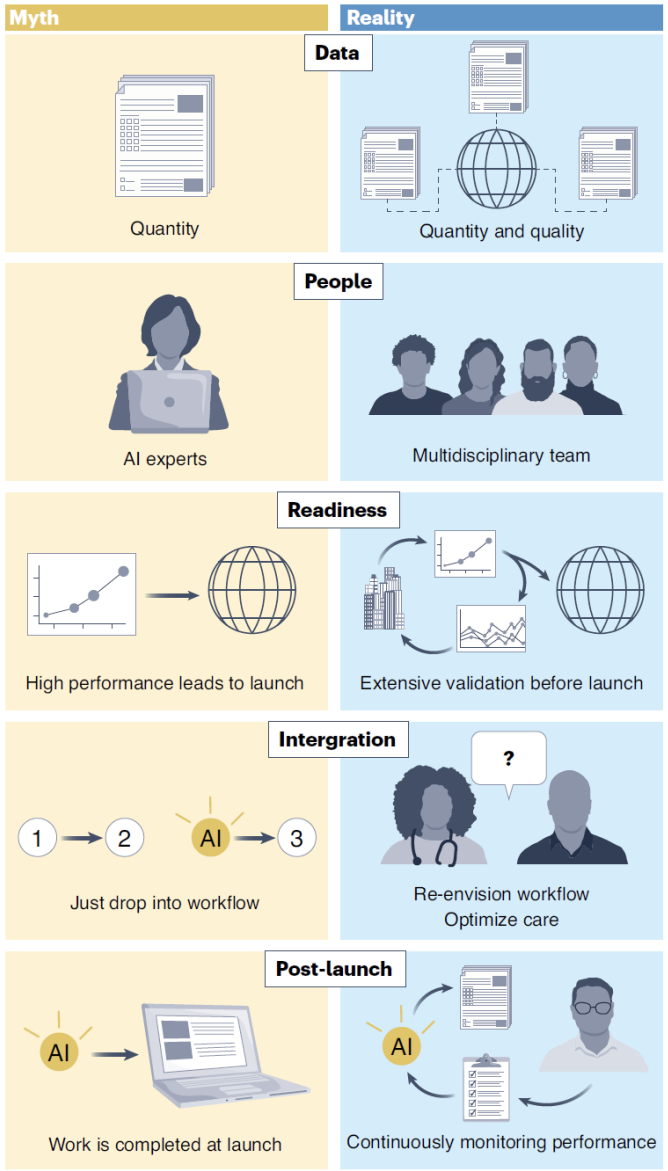
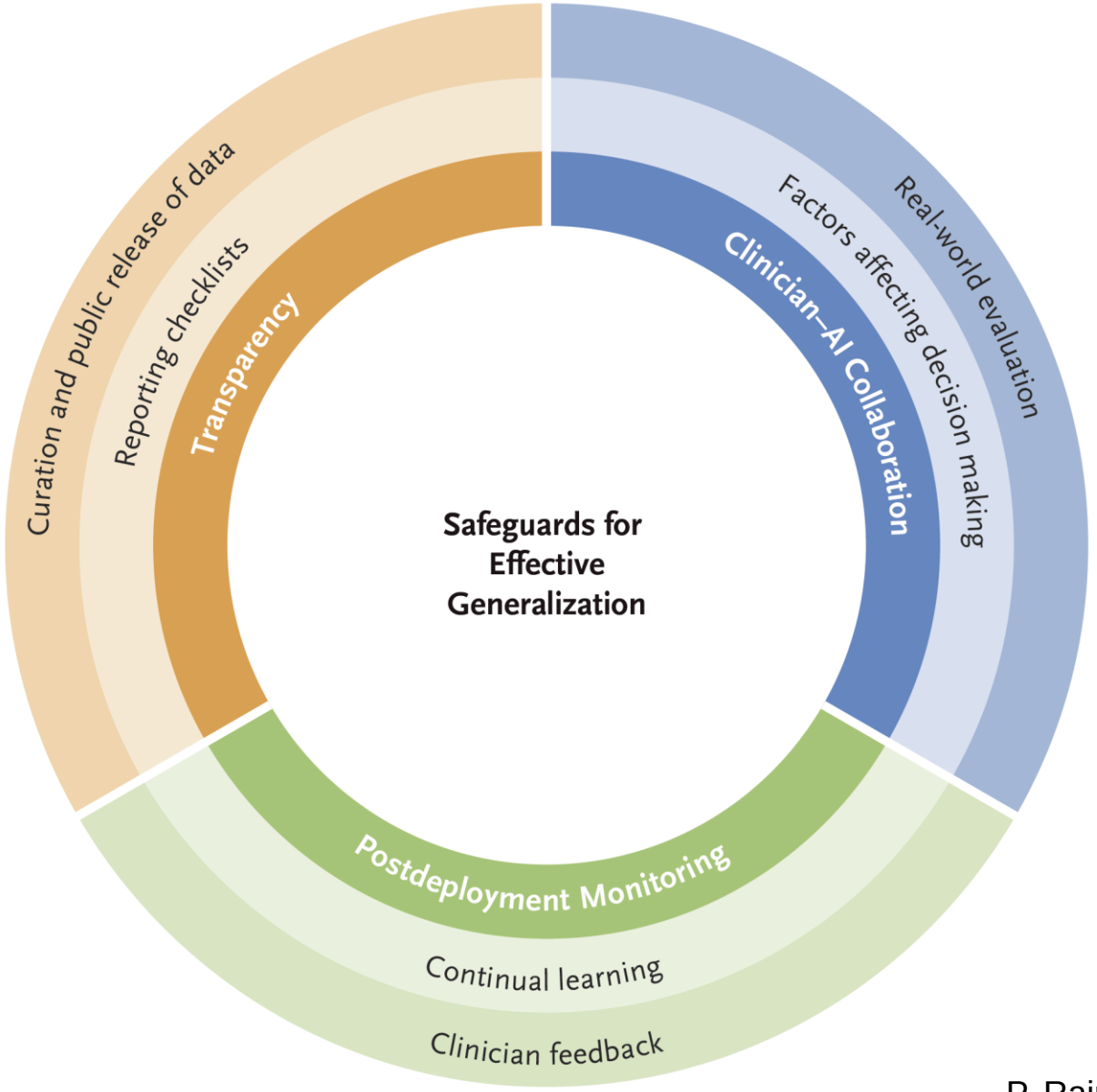


Table 1 | Myths and reality in developing medical AI

Myth	Reality
More data means better AI models	Although adequate data volume is important for developing an accurate AI model, data and label quality matters more[3], especially as the quantity becomes less critical as AI advances[17,18].
Only AI experts are needed	Although AI experts are core contributors in developing medical AI models, building a complete, well-functioning AI system takes a village of multidisciplinary team members.
AI performance leads to clinical confidence	Building users' confidence in using medical AI takes time and careful validations.
Integrating AI into routine workflows is straightforward	AI should be designed around humans, not the other way around.
Launch means success	Ensure AI's high-quality performance through continuous monitoring and iterations.

K. Widner et al., Nature Medicine 2023, 29, 1304-1306

Generalization Checks for AI Systems



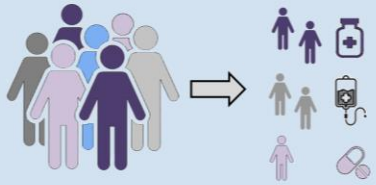
P. Rajpurkar et al., N Engl J Med 2023;388:1981-90

AI in Hematology & Oncology

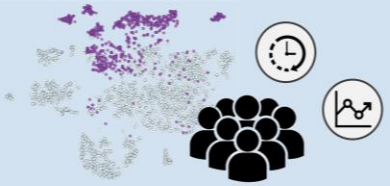
Fields of Application

early and accurate diagnosis

treatment planning and personalization



outcome prediction and prognostication



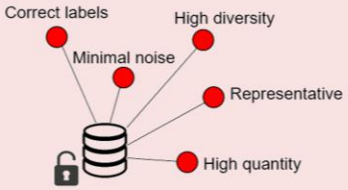
treatment monitoring and adverse event detection

clinical decision support

streamlined workflows and resource optimization

Requirements

Data availability

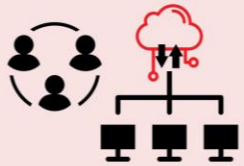


Data quality

ethical and regulatory compliance

validation and regulatory approval

infrastructure and computational resources



collaboration and interdisciplinary expertise

user training and education

continuous monitoring and improvement

Sehr viele Modelle für diverse Anwendungen entwickelt

Herausforderung/ nächste Schritte:

- Umfassende Validierungen
- Wissenstransfer für Akzeptanz im klinischen Umfeld