

Automated Analysis of Her2/neu Samples with Metafer MetaCyte *PV*

Dr. Christian Schunck
MetaSystems Germany



10th European Congress on Telepathology
4th International Congress on Virtual Microscopy
Vilnius, Lithuania



System Architecture

Slide Feeder for up
to 80/500 Slides

8-Slides
Motorized Stage

Research Microscope
(CZ AxioImager Z2)
w/ FL Illumination

High-res. b/w
CCD Camera

Windows Compatible
PC with Metafer PV
Software

Printer and Peripherals



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History of Metafer PV System

2000

- Collaboration of Abbott's Vysis and MetaSystems to develop an automated, FDA approved system to analyze PathVysion™ samples
- Development of a PV analysis system based on the Metafer platform ("*Metafer PV*")
- Analysis of ~1,000 samples
(*2 training data sets, 1 independent test data set*)

2005

- FDA approval for the "*AutoVysion*" system to analyze PathVysion™ Her2 DNA probe kit samples

2006

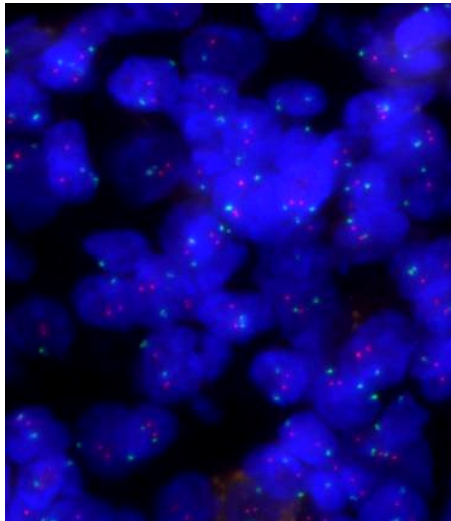
- Final agreement between Vysis and MetaSystems on marketing the *AutoVysion / Metafer PV* systems



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Her2/neu Analysis Strategy



1. Interactive selection of tumor regions by a trained pathologist

Mark Fields

Her2	10	No	ID	S	X
PathVysion V2-	40x	1	1		-850
		2	2		646
		3	3		3555
		4	4		7158
		5	5		4551
		6	6		2134
		7	7		5255
		8	8		7801
		9	9		11599
		10	10		14889

X: 14889
Y: 19248

Delete Reject Record Undo

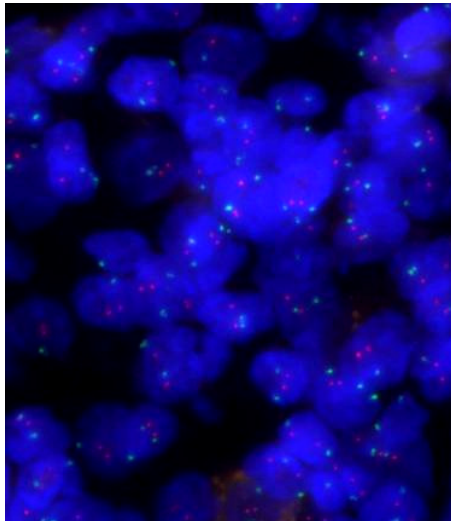
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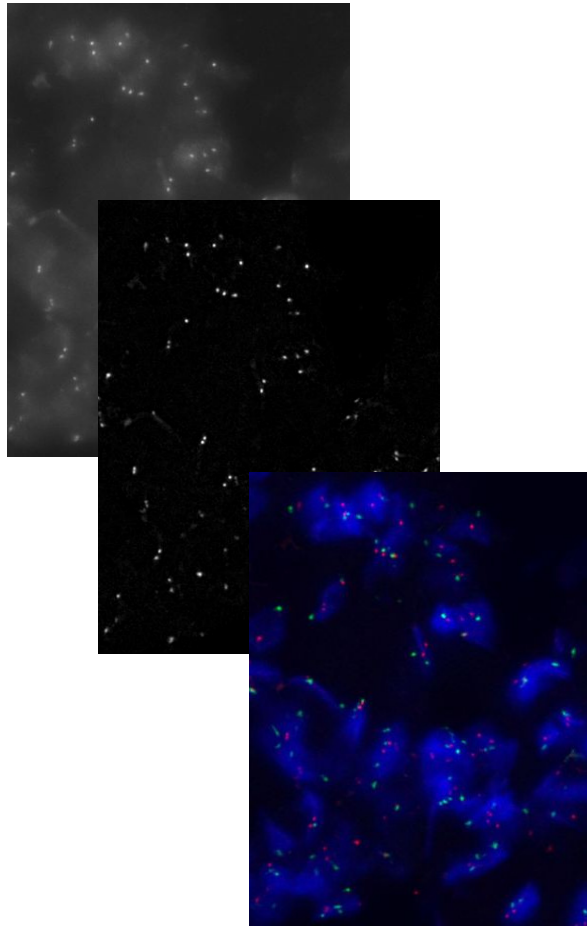
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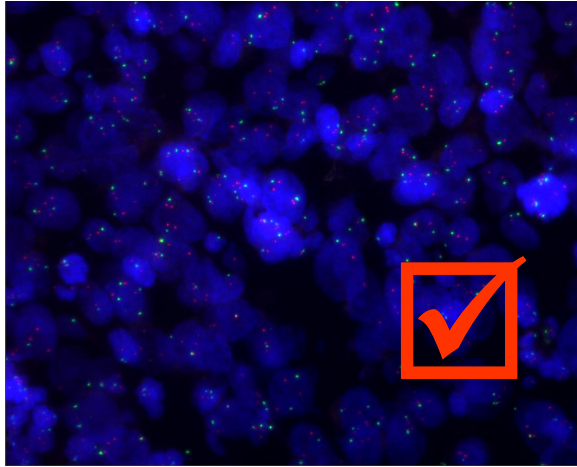
1. Interactive selection of tumor regions by a pathologist
2. Automated image acquisition with 9 focus planes (signal channels only), and generation of extended focus image; image processing



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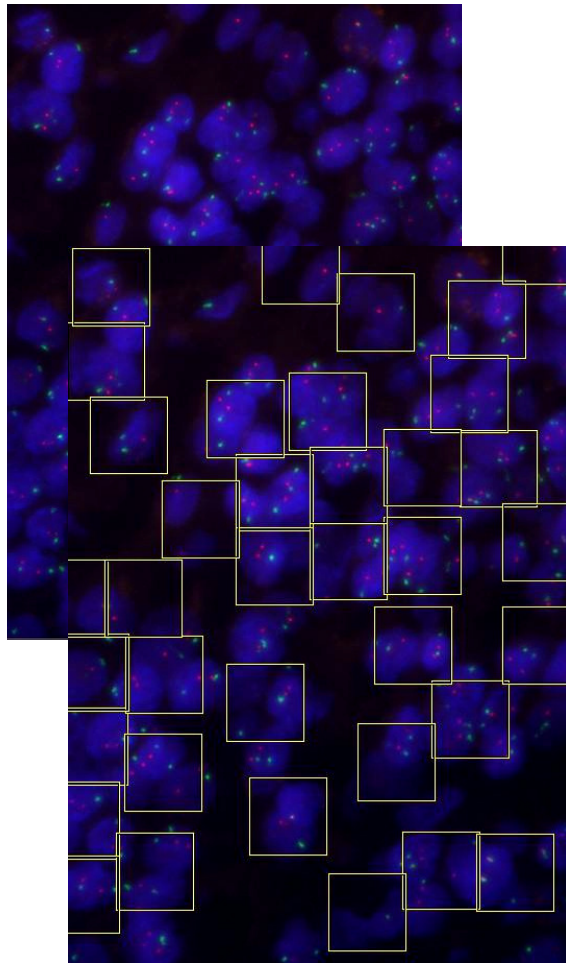
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3. Automated rejection of FOVs based on image quality (backgr. cond., signal presence)



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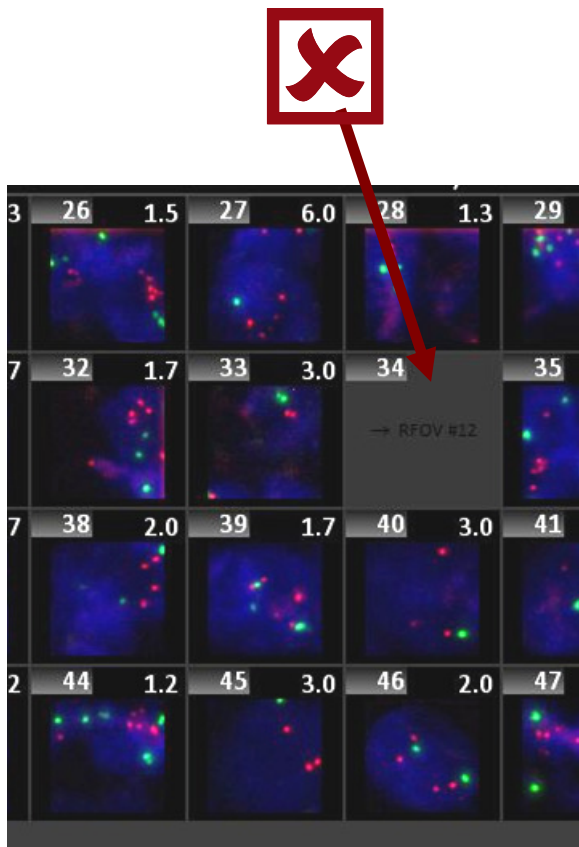
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4. **‚Tile Sampling‘: cells / ROIs are detected in the DAPI channel**



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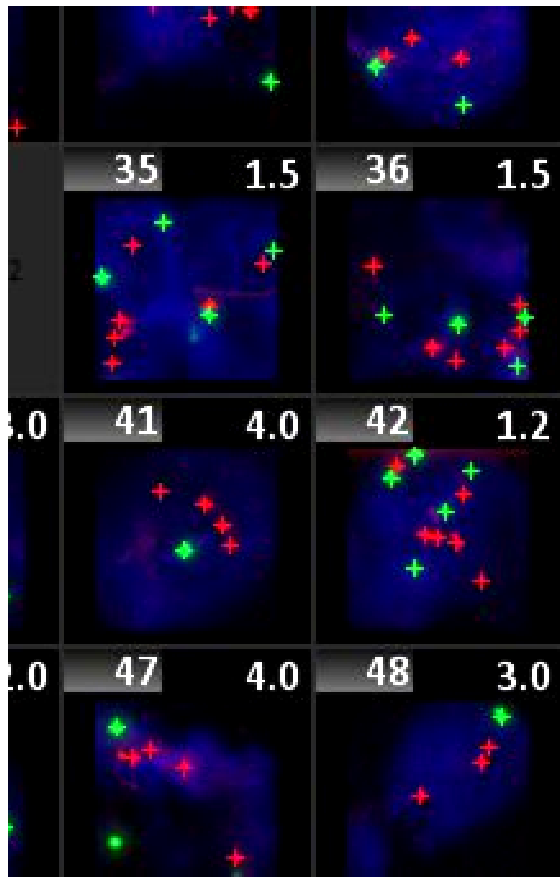
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5. **Automated rejection of tiles based on image quality**



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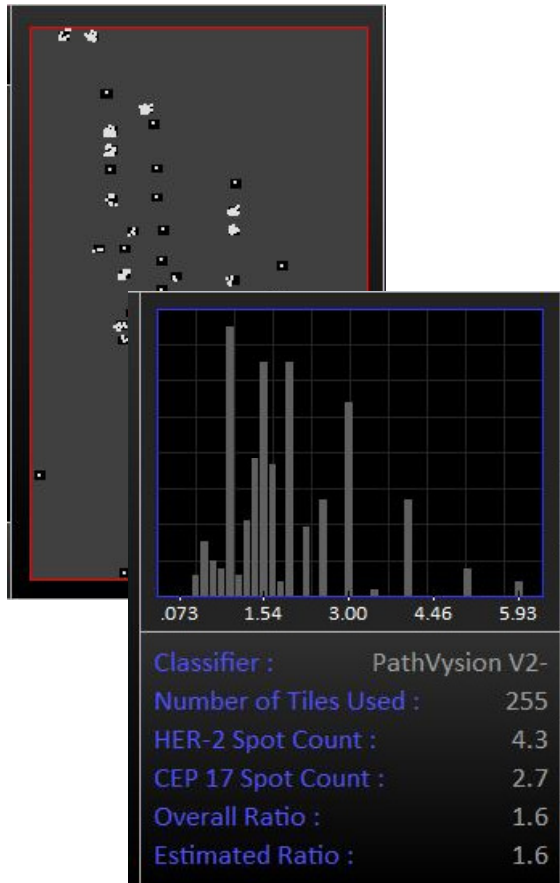
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6. **Signal count / automated detection of HSRs**



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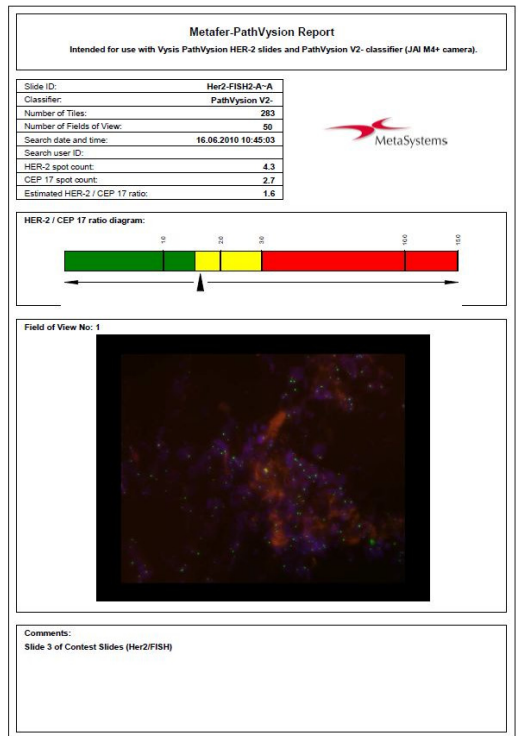
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2. Automated image acquisition with 9 focus planes (signal channels only), and generation of extended focus image; image processing
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4. ‚Tile Sampling‘: cells / ROIs are detected in the DAPI channel
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6. Signal count / automated detection of HSRs
- 7. Data summary and display on screen**



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4. ‚Tile Sampling‘: cells / ROIs are detected in the DAPI channel
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6. Signal count / automated detection of HSRs
7. Data summary and display on screen
- 8. Reporting**

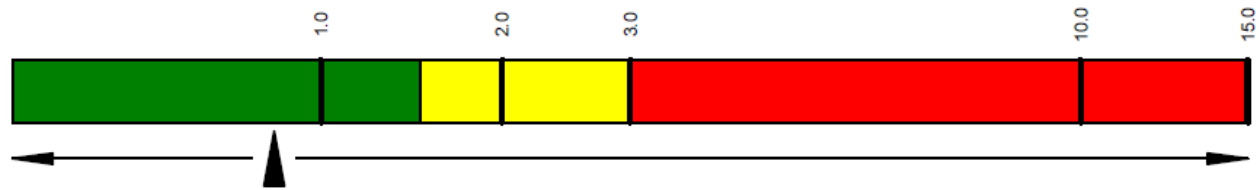


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Results

HER-2 / CEP 17 ratio diagram:



Non-amplified sample: Contest Sample No. 5

HER-2 / CEP 17 ratio diagram:



Ambiguous sample: Contest Sample No. 1



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Contest Slides Data

No.	No. of Analyzed Tiles	Her2 Signal Count	CEP17 Signal Count	Overall Ratio	Amplified
1	210*	(3.9)	(1.7)	(2.2)	Ambiguous
*FOVs and ROIs (tiles) did not pass the quality test. Rejection criteria were disabled, and manual tiles rejection has been done.					
2	255	4.3	2.7	1.6	Ambiguous
3	1285	3.5	2.3	1.5	No (Ambiguous)
4	102	3.8	6.6	0.6	No
5	95	2.7	3.2	0.8	No



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References

- Analysis of HER2 gene amplification using an automated fluorescence in situ hybridization signal enumeration system.
Stevens et al., J Molecular Diagn 9(2007)
- New cutpoints to identify increased HER2 copy number: analysis of a large, population-based cohort with long-term follow-up.
Jensen et al., Breast Cancer Res Treat 3(2008)
- High concordance between immunohistochemistry and fluorescence in situ hybridization testing for HER2 status in breast cancer requires a normalized IHC scoring system.
Gown et al., Mod Pathol 10(2008)



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