

Jornadas *Ventana Digital Pathology*

because
every second
counts



Barcelona 18/19 de octubre de 2012

Barcelona 18/19 de octubre de 2012

Barcelona 18/19 de octubre de 2012

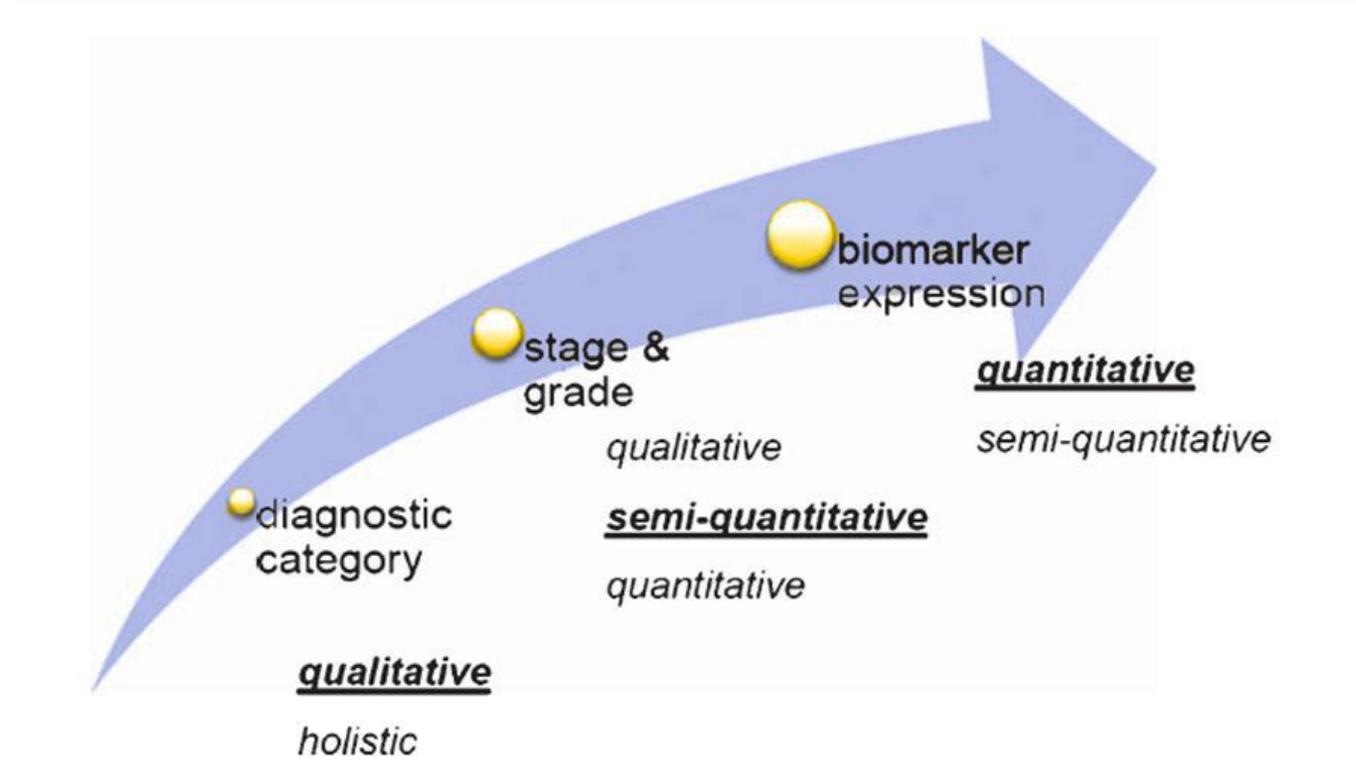
Uso de algoritmos automatizados en diagnóstico clínico

Federico Rojo

Benefits of digital analysis in pathology: increased demand for quantification

- Determining markers (i.e. ER, PR & HER-2/neu in breast cancer) for prognostic & predictive purposes by IHC and/or FISH is the standard of practice.
- IHC score/quantification by manual microscopy is currently accepted as the traditional gold standard.
- Surgical Pathology workflow involves:
 - **Pre-analytic preparation** (tissue fixation & processing)
 - **Analysis** (method)
 - **Post-analytical component** (quantification & reporting)
- Discrepancies between HER2 IHC & FISH mainly reflect errors in manual interpretation.
- Inter- and intra-observer differences in scoring occur:
 - Most notably with borderline & weakly stained cases
 - Related to fatigue & subjectivity of human observers

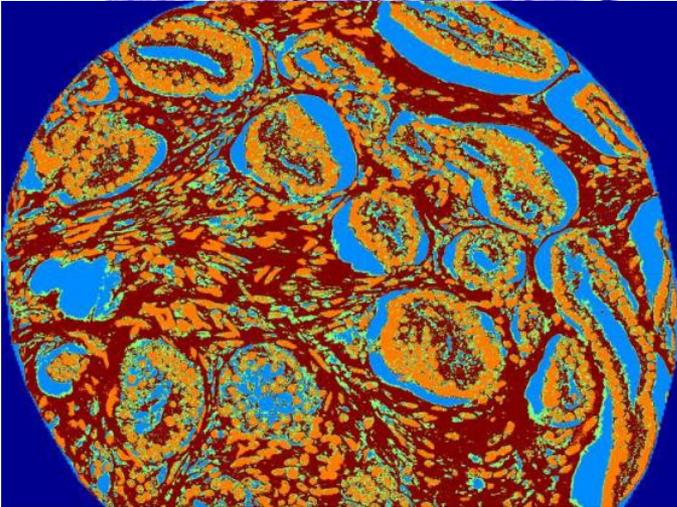
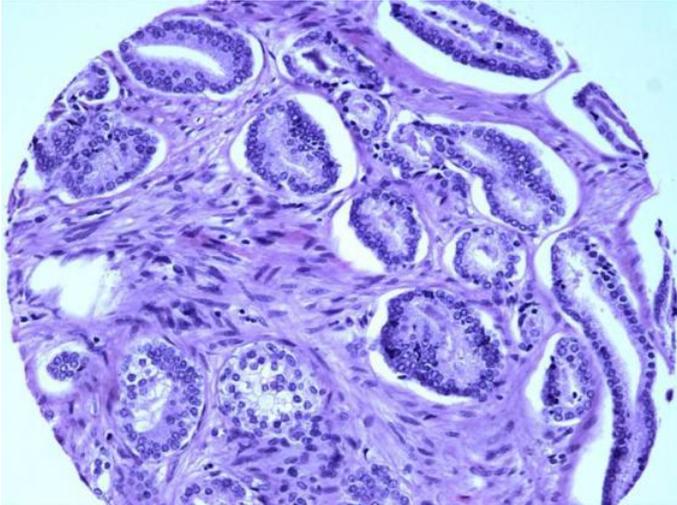
Benefits of digital analysis in pathology: increased demand for quantification



The brain of a pathologist

Complexity for developing algorithms:

Image segmentation, Image analysis and Computational modeling



For all objects do	Merge regions based on size
$D_o \leftarrow$ GWDT of object o	until all regions are valid nuclei
$h \leftarrow 0$	$M_h \leftarrow$ merged W_h
$S_{min} \leftarrow \infty$	$m \leftarrow$ # of regions after merge
$m \leftarrow$ # initial regions	$S_h \leftarrow$ calculate S on merged W_h
while $m > 1$ do	if $S_h < S_{min}$ then
repeat	$M_{h+1} \leftarrow M_h$
$h \leftarrow h+1$	$S_{min} = S_h$
$H_h \leftarrow$ H-minima of D_o	end if
until # region minima of $H_h < m$	end while
$W_h \leftarrow$ Watershed transform of H_h	Separation of object $o \leftarrow M_{h+1}$
repeat	end for

$$F = \beta_s \int_{\Omega} (\phi(x) - \psi(x))^2 dx + \underbrace{\beta_r \int_{\Omega} \Theta_m H_{in} H_{\phi} dx + \int_{\Omega} \Theta_{out} H_{\phi} dx}_{\text{Region force}}$$

$$F(\Phi, \Psi, u_m, u_{mem}) = \beta_s \int_{\Omega} \Theta_m H_{in} H_{\phi} dx + \int_{\Omega} \Theta_{out} H_{\phi} dx + \omega \int_{\Omega} H_{in} H_{\phi} dx + \sum_{i=1}^2 \int_{\Omega} (\phi_i - \psi_i)^2 dx$$

$$\frac{\partial \phi}{\partial t} = \delta \phi \left[\mu \nabla \cdot \left(\frac{\nabla \phi}{|\nabla \phi|} \right) - (((f - u_m)^2 + (f - u_{mem})^2)(1 - H_{\phi})) \right] - 2\nu(\phi - \psi_i)$$

$$\frac{\partial \phi}{\partial t} = 2\nu \int_{\Omega} (\phi - \psi_i) (\nabla \psi_i \cdot \nabla \phi) dx$$

$$\frac{\partial \psi_i}{\partial t} = 2\nu \int_{\Omega} (\phi - \psi_i) (\nabla \psi_i \cdot \nabla \psi_i) dx$$

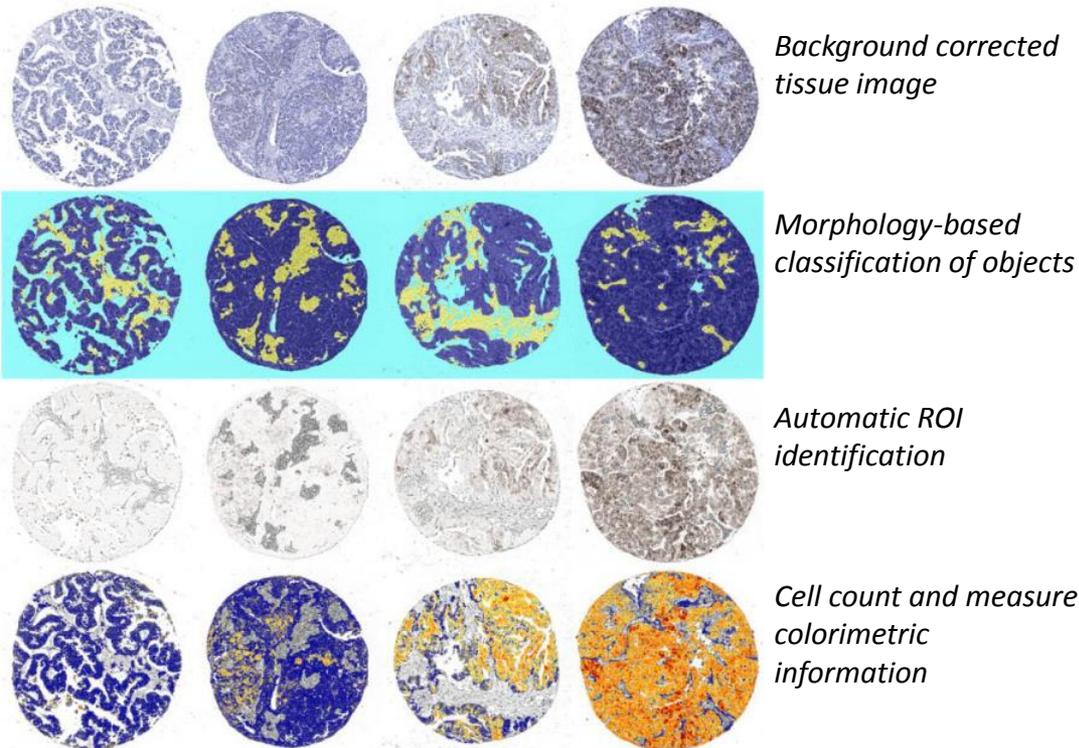
$$\frac{\partial \psi_i}{\partial t} = 2\nu \int_{\Omega} (\phi - \psi_i) \left(-\frac{\psi_i}{s} + \nabla \psi_i \cdot \nabla A_i \right) dx$$

$$i, j \in \{1, 2\}, i \neq j$$

Quantitative tissue analysis
 Hundreds of measurements
 Components include: size, shape, color, texture, relationships to each other

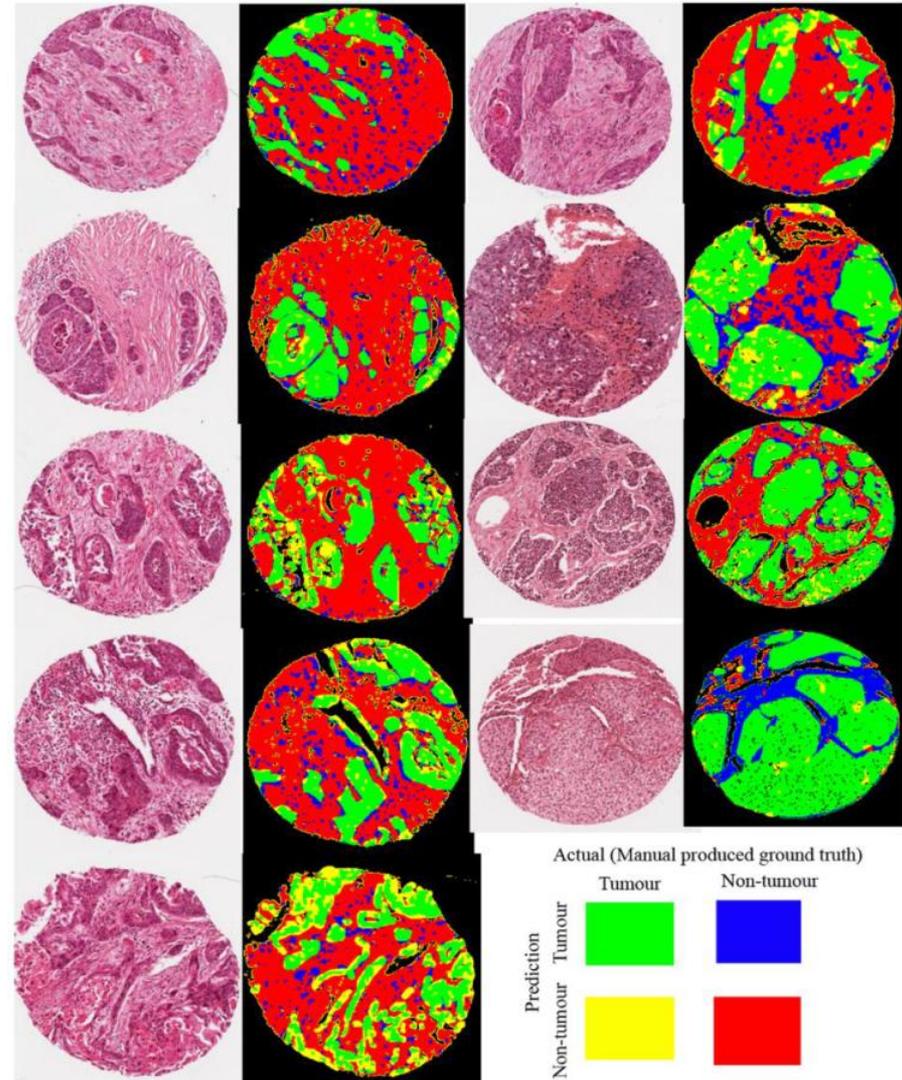
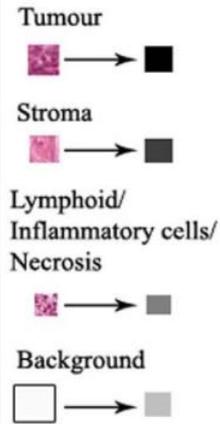
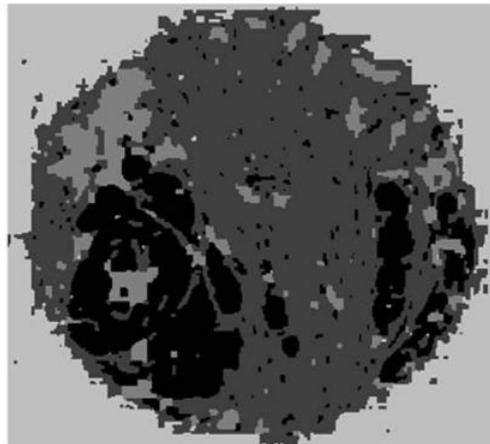
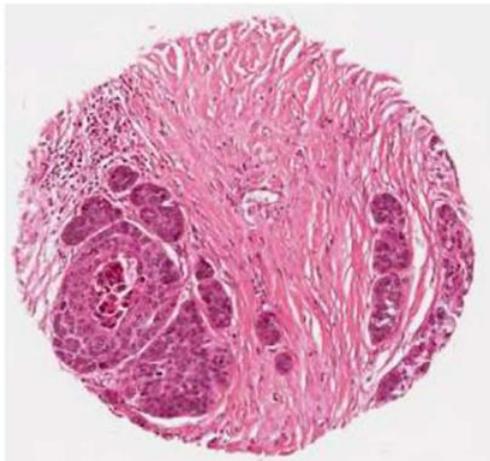
Area	Number of Vessel None	Rel. border to Cell Negative
Length	Number of Vessel Small	Rel. border to Cell Small
Length/width	Number of Vessel Wall	Rel. border to Cell not colocalized
Number of pixels	Number of Vessel with Lumen	Rel. border to Cytoplasm
Width	Number of Vessel without Lumen	Rel. border to Hematoxylin
Circularity	Number of unclassified	Rel. border to Marker Areas
Compactness	Border to Background	Rel. border to Marker High
Density	Border to Cell	Rel. border to Marker Low
Ellipticity	Border to Cell High	Rel. border to Marker Medium
Roundness	Border to Cell Large	Rel. border to Marker Stain (IHC)
Shape index	Border to Cell Low	Rel. border to Membrane
Distance to scene border	Border to Cell Medium	Rel. border to Membrane none
Mean Brown Chromogen Intensity	Border to Cell Negative	Rel. border to Membrane strong
Mean Hematoxylin Intensity	Border to Cell Small	Rel. border to Membrane weak
Optical Density	Border to Cell not colocalized	Rel. border to Nucleus
Cell Cytoplasm/Nucleus Intensity Ratio	Border to Cytoplasm	Rel. border to Nucleus High
Cell Membrane/Cytoplasm Contrast	Border to Hematoxylin	Rel. border to Nucleus Large
Cytoplasm Subobject Brown Chromogen	Border to Marker Areas	Rel. border to Nucleus Low
Cytoplasm Subobject Optical Density	Border to Marker High	Rel. border to Nucleus Medium
Membrane Subobject Brown Chromogen	Border to Marker Low	Rel. border to Nucleus Negative
Membrane Subobject Optical Density	Border to Marker Medium	Rel. border to Nucleus Positive
Nucleus Subobject Brown Chromogen	Border to Marker Stain (IHC)	Rel. border to Nucleus Small
Nucleus Subobject Optical Density	Border to Membrane	Rel. border to Nucleus colocalization subclasses
Cell Membrane/Cytoplasm Intensity Ratio	Border to Membrane none	Rel. border to Nucleus not colocalized
Number of Background	Border to Membrane strong	Rel. border to Nucleus not colocalized
Number of Cell	Border to Membrane weak	Rel. border to Vessel
Number of Cell Colocalization Subclasses	Border to Nucleus	Rel. border to Vessel High
Number of Cell Markers colocalized	Border to Nucleus High	Rel. border to Vessel Large
Number of Cell Medium	Border to Nucleus Large	Rel. border to Vessel Low
Number of Cell Negative	Border to Nucleus Low	Rel. border to Vessel Lumen
Number of Cell Small	Border to Nucleus Medium	Rel. border to Vessel Medium
Number of Cell not colocalized	Border to Nucleus Negative	Rel. border to Vessel None
Number of Cytoplasm	Border to Nucleus Positive	Rel. border to Vessel Small
Number of Hematoxylin	Border to Nucleus Small	Rel. border to Vessel Wall
Number of Marker Areas	Border to Nucleus colocalization subclasses	Rel. border to Vessel with Lumen
Number of Membrane	Border to Nucleus not colocalized	Rel. border to Vessel without Lumen
Number of Membrane none	Border to Vessel	Rel. border to unclassified
Number of Membrane strong	Border to Vessel High	Number of Cytoplasm
Number of Membrane weak	Border to Vessel Large	Number of Membrane
Number of Nucleus	Border to Vessel Low	Number of Nucleus
Number of Nucleus High	Border to Vessel Lumen	Number of Nucleus Lumen
Number of Nucleus Large	Border to Vessel Medium	Number of Nucleus Wall
Number of Nucleus Low	Border to Vessel None	Number of Vessel Wall
Number of Nucleus Medium	Border to Vessel Small	Area of Cytoplasm
Number of Nucleus Negative	Border to Vessel Wall	Area of Membrane
Number of Nucleus Positive	Border to Vessel with Lumen	Area of Nucleus
Number of Nucleus Small	Border to Vessel without Lumen	Area of Vessel Lumen
Number of Nucleus colocalization subclasses	Border to unclassified	Area of Vessel Wall
Number of Nucleus not colocalized	Rel. border to Background	Rel. area of Cytoplasm
Number of Vessel	Rel. border to Cell	Rel. area of Membrane
Number of Vessel High	Rel. border to Cell Colocalization Subclasses	Rel. area of Nucleus
Number of Vessel Low	Rel. border to Cell High	Rel. area of Vessel Lumen
Number of Vessel Lumen	Rel. border to Cell Large	Rel. area of Vessel Wall
Number of Vessel Medium	Rel. border to Cell Low	Classified as Background
		Classified as Cell
		Classified as Cell Colocalization Subclasses
		Classified as Cell High

Automated tumor segmentation on tissue images: How the algorithm works on IHC



- Object-Oriented Image Analysis (morphology- based)
- Involves color normalization, background extraction, segmentation, classification & feature selection
- Separation of tissue elements (e.g. tumor epithelium) from background (e.g. stroma) permits selection of areas of interest & filtering out of unwanted areas
- Region of Interest (ROI) is subject to further image analysis (computation of diagnostic score)
- Quantification of results

Automated tumor segmentation on tissue images



Companion and public automated analysis algorithms

	ImageJ	Enhanced Cell Classifier and Cell Profiler	MatLab7	DetecTiff	AQUA	HER2-Connect	ACIS	InScan	Pathiam /Virtuoso	Tripath	Applied Spectral Imaging	Duet System	Cell Analysis	Slidepath Tissue IA	Nuance Maestro	TissueMap
Source	NIH	SVM	Mathworks	Labview	HistoRx	Visiopharm	Chromavis ion, Dako	ScanScope , Aperio	Biolmagen e/Ventana -Roche	Ventana-Roche	Ariol	CompuCyt e	Bitplane	Slidepath Tissue	CRi (Caliper)	Definiens
Applications	Thousands (pluggins for ER, PR, HER2, ISH and Ki67)	ER, PR, HER2	ER, PR, HER2	ER, PR, HER2	Hundreds (ER, PR, HER2)	HER2	HER2	ER, PR, HER2	ER, PR, HER2, p53, Ki67, ISH	HER2, Ki67	ER, PR, HER2, FISH	FISH HER2	ER, PR	ER, PR, HER2, p53, Ki67, ISH	Hundreds (ER, PR, HER2)	Hundreds (ER, PR, HER2)
FDA-cleared (FDA510k)	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No

25 years of bioimage analysis: From NIH Image to ImageJ

Table 1 | List of NIH Image and ImageJ variants

	Date initiated	Description
NIH Image	1987	The predecessor of ImageJ, created by Rasband; made for the Macintosh; no longer under active development
ImageSXM	May 1993	A version of NIH Image for OSX extended by Steve Barrett; intended to handle loading, display and analysis of images from the scanning microscope
ImageJ	1997	The current version of ImageJ developed by Rasband; sometimes called ImageJ1
ImageJ2x	Unknown	An offshoot of ImageJ; modified to use Swing interface; no longer under active development
ImageJA	July 2005	An offshoot of ImageJ developed by Johannes Schindelin; used as the core of Fiji
Fiji	December 2007	A 'batteries included' distribution of ImageJ popular in the life sciences
ImageJX	March 2009	Created by Grant Harris to discuss improvements to ImageJ; formed the basis of an application to NIH that launched ImageJDev
ImageJ2 (ImageJDev)	December 2009	Under development by the ImageJDev project; a complete rewrite of ImageJ; includes ImageJ1 to allow for old-style plug-ins and macros
MBF_ImageJ	2005	Bundle developed by Tony Collins for light microscopists; plug-ins from MBF_ImageJ can be installed on Fiji, combining the programs
SalsaJ	Unknown	An offshoot of ImageJ intended for astronomy applications; designed for use in classrooms; available in over 30 languages
CellProfiler	2006	Free, open-source software started by Anne Carpenter and Thouis Jones; aids biologists without computer-vision training to quantitatively measure cell images automatically
Icy	2011	Created by the Quantitative Image Analysis Unit at Institut Pasteur, Icy provides integrated software to bridge the gap between users and developers through open-source software and a central website
Bio7	Unknown	Application used for ecological modeling; integrated development environment; focuses on individual-based modeling and spatially explicit models
µManager	2005	Open-source microscopy software; controls automated microscopes; comprehensive imaging solution when used with ImageJ; developed by Arthur Edelstein, Ziah Dean, Henry Pinkard and Nico Stuurman

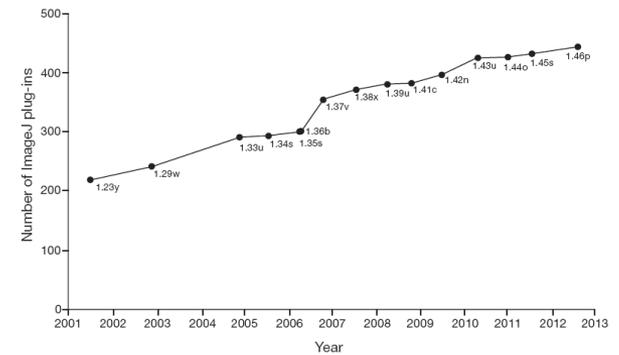
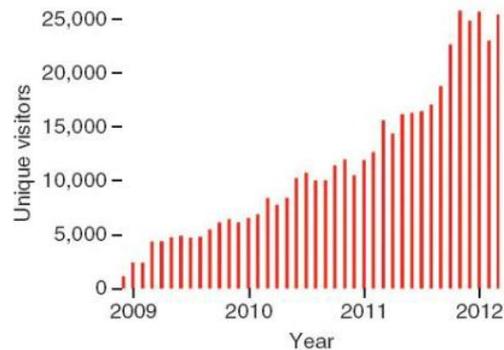


Figure 2 | ImageJ plug-ins bundled with each ImageJ release over time. Each data point is labeled with the version number and letter.

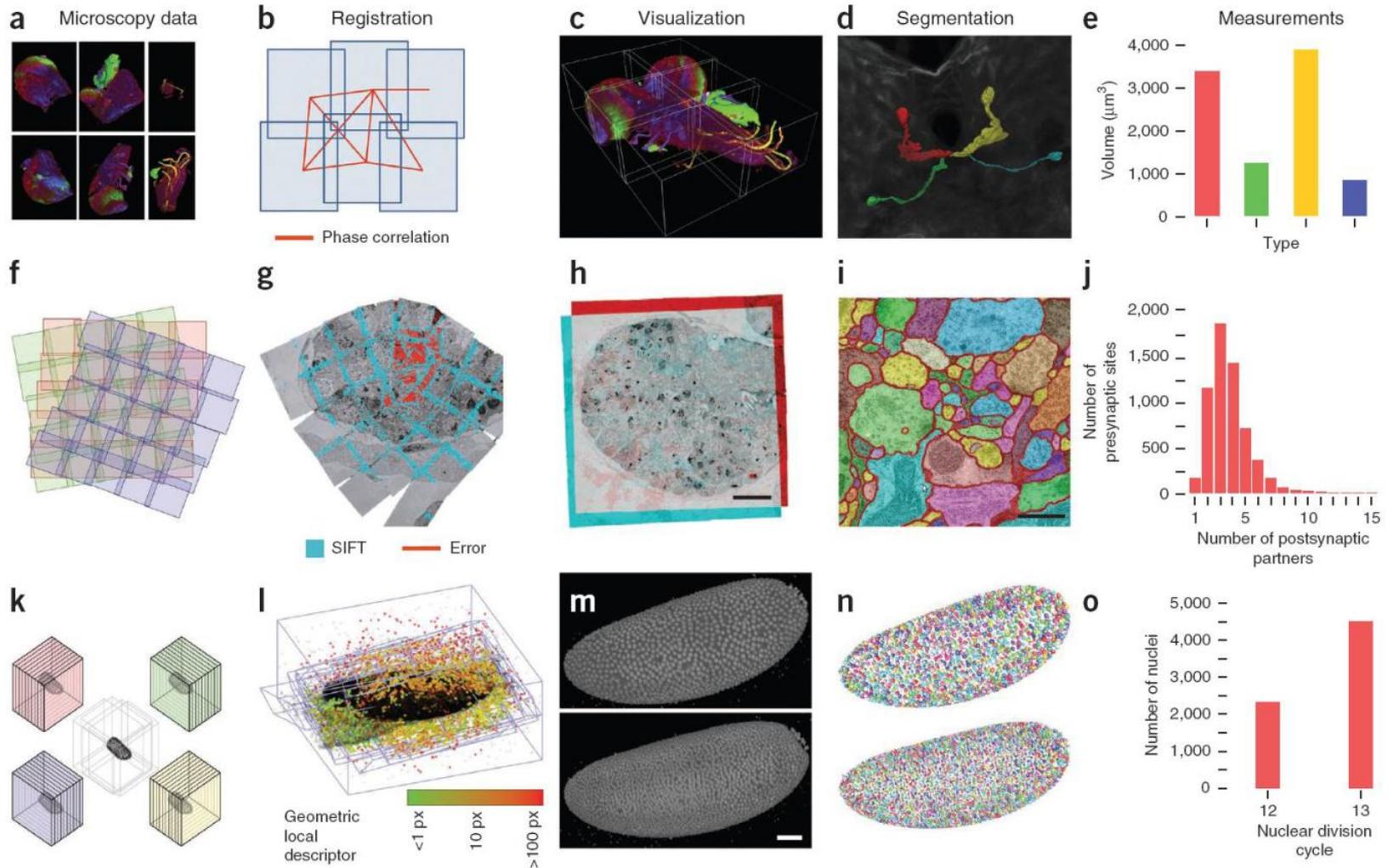
Unique visitors over the last three years



World map with locations of updated 2012 ImageJ



25 years of bioimage analysis: From NIH Image to ImageJ



Membrane connectivity: algorithm evaluation for HER2 immunohistochemistry in breast cancer

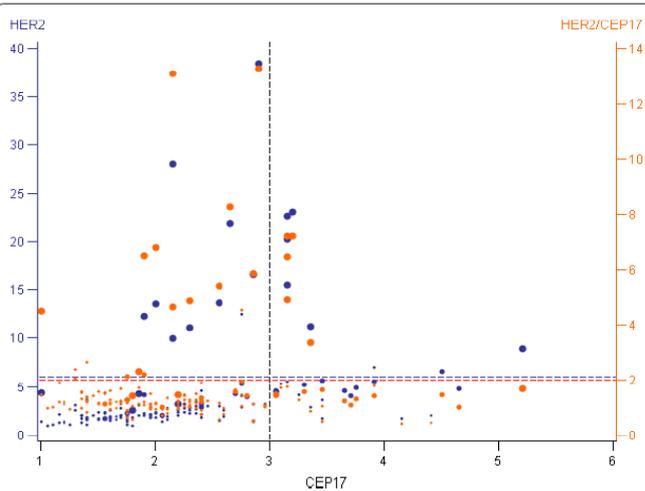


Figure 3 Bubble plot display of interrelationship between the HER2 membrane connectivity estimate and HER2 FISH data.

Horizontal axis represents mean CEP17 by FISH analysis. Left vertical axis represents mean HER2 by FISH analysis. Right vertical axis represents HER2/CEP17 ratio. Bubble size is proportional to the patient's maximum HER2 connectivity value. Black dashed vertical reference line separates cases with polysomy (CEP17 > 3) to the right. Blue and orange dashed horizontal reference lines separate cases with amplification (HER2 > 6 and HER2/CEP17 > 2) above. Each patient is represented by two bubbles with the same CEP17 value: blue bubble maps to the mean HER2 orange bubble - to the mean HER2/CEP17 ratio.

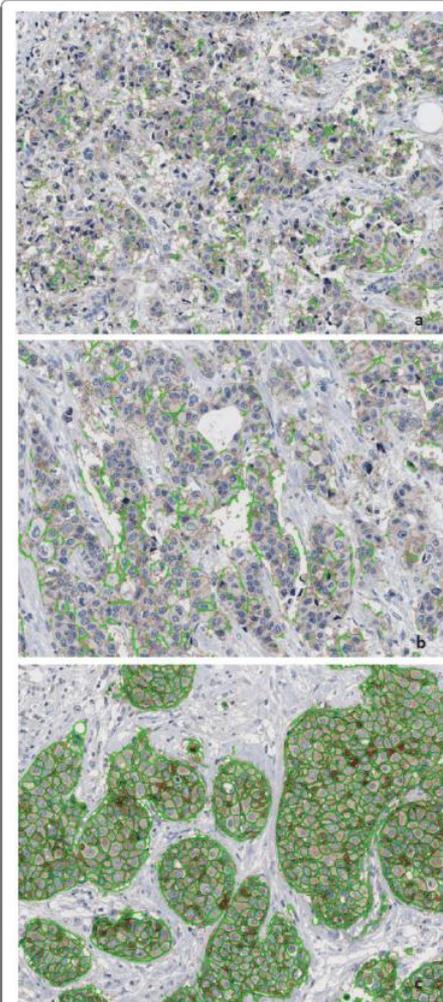
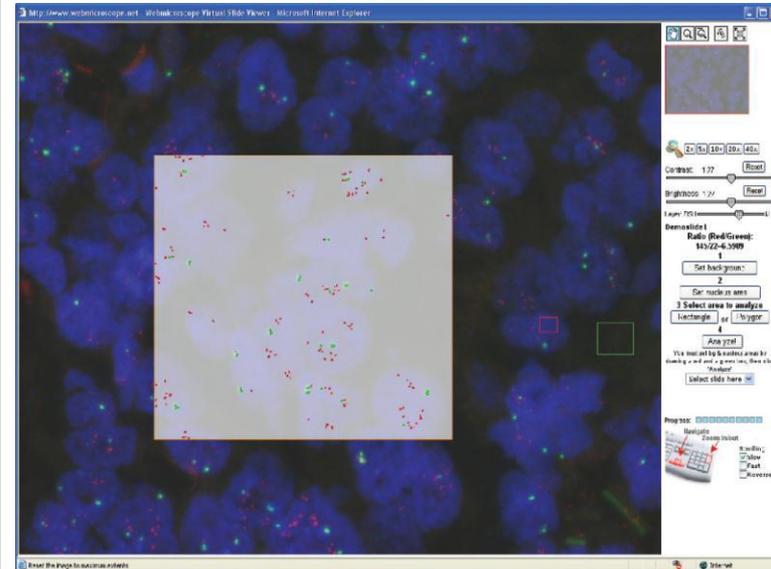
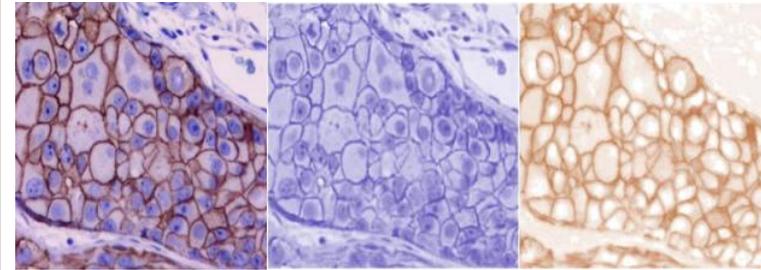
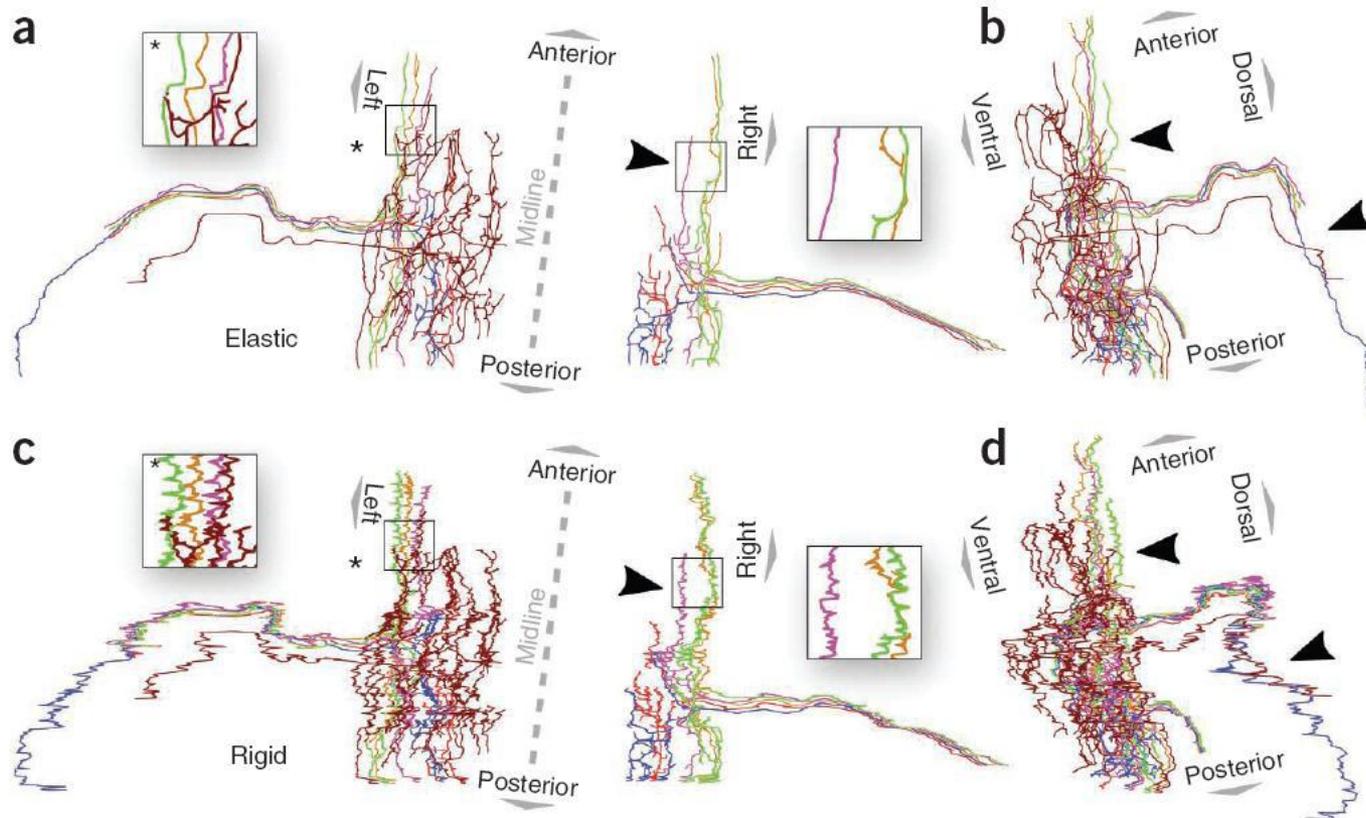


Figure 1 Image outputs of the digital analyses. Tissue microarray images scored by digital analysis as 0/1+ 2+ and 3+ (a, b, and c, respectively); green lines outline cell membranes revealing positive HER2 immunohistochemical staining by membrane connectivity estimate.



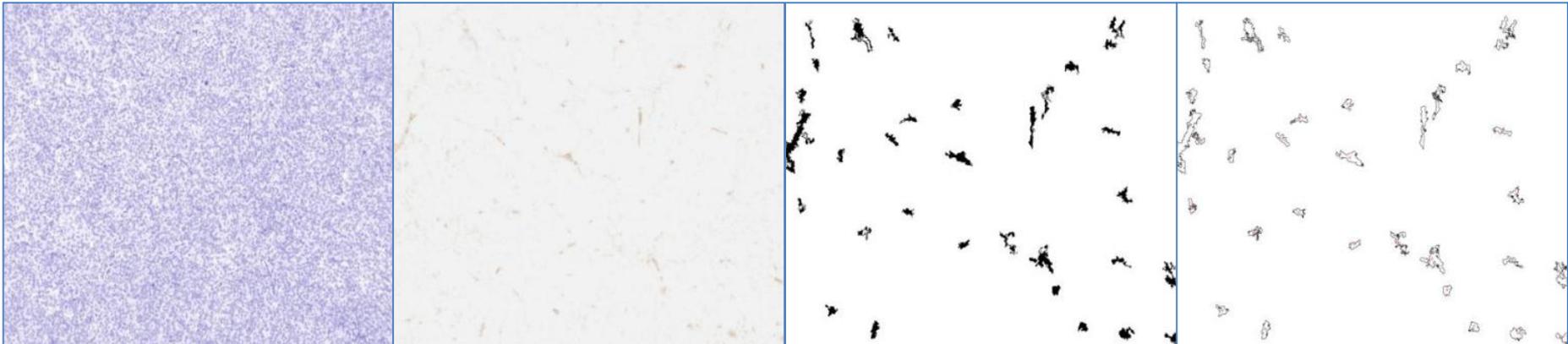
25 years of bioimage analysis: From NIH Image to ImageJ

Reconstructed neuronal arbors

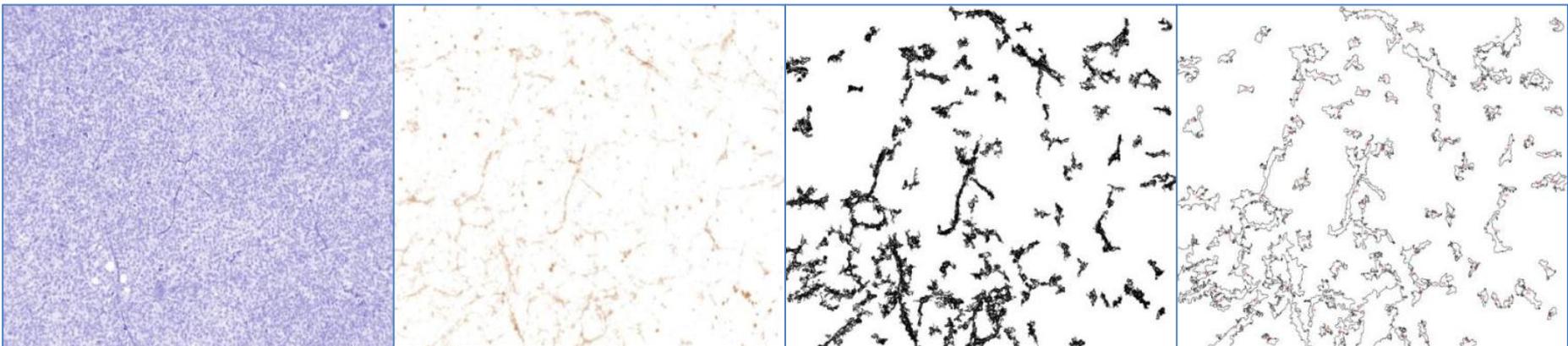


Automated microvascular density measurement: Neuronal tracer algorithm for CD31-shapes

H69



H69M



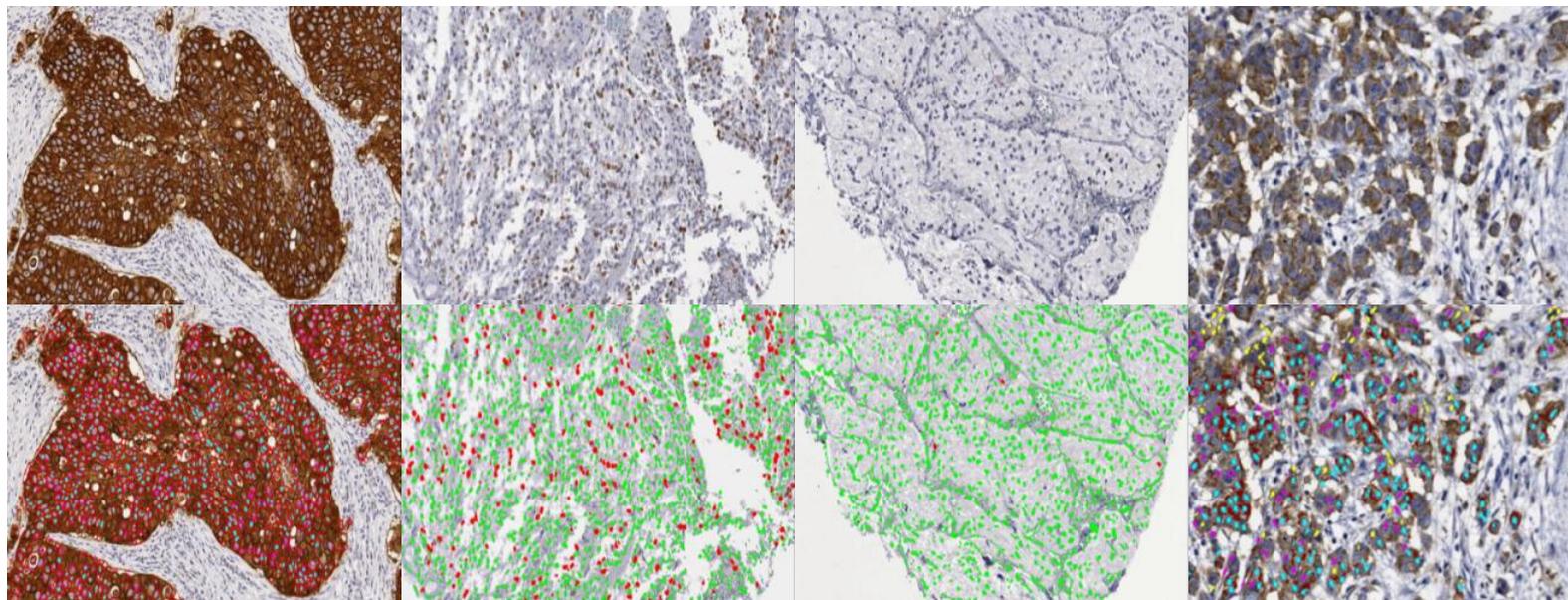
Hematoxylin

DAB

Masks

Outlines and count

Automated recognition of staining patterns in tumor on complete section



User Input

Magnification

Nucleus Identification

Size

Radius

Brightness

Center Identification Mask

Identification by Size (Sigma)

Epithelial Area Identification

Epithelial Area

Epithelial Intensity

Circularity Of Nucleus

Non Stained Nuclei Filter

Nuclei Elongation Ratio

Minimum Nucleus Size

Cytoplasm Identification

Cytoplasm Staining

Cytoplasm Staining Percentage

0+ Cells	0 to 10	<input type="text" value="10"/>
1+ Cells	10 to 40	<input type="text" value="40"/>
2+ Cells	40 to 80	<input type="text" value="80"/>
3+ Cells	80 to 100	<input type="text" value="80"/>

Cytoplasm Staining Score Clustering

Score 3	Range	<input type="text" value="30"/>
3+ Cells	30 to 100	Or <input type="text" value="80"/>
Score 2	80 to 100	Or <input type="text" value="10"/>
3+ Cells	10 to 30	Or <input type="text" value="30"/>
Score 1	30 to 80	Or <input type="text" value="10"/>
2+ Cells	10 to 30	Or <input type="text" value="5"/>
1+ Cells	5 to 100	Or <input type="text" value="0"/>
Score 0	0 to 100	
0+ Cells		

Analyze Defaults Sets Save Reset

Legends for Antibody : S6

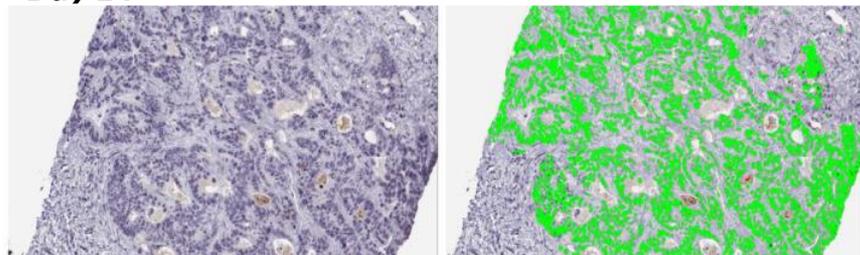
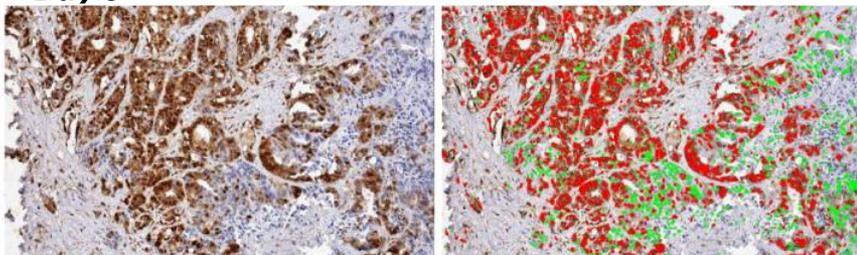
<input type="checkbox"/>	Zero Plus Cells	<input type="button" value="Close"/>
<input type="checkbox"/>	One Plus Cells	
<input type="checkbox"/>	Two Plus Cells	
<input type="checkbox"/>	Three Plus Cells	
<input type="checkbox"/>	Cytoplasm	

Automated recognition of staining patterns in tumor on complete section

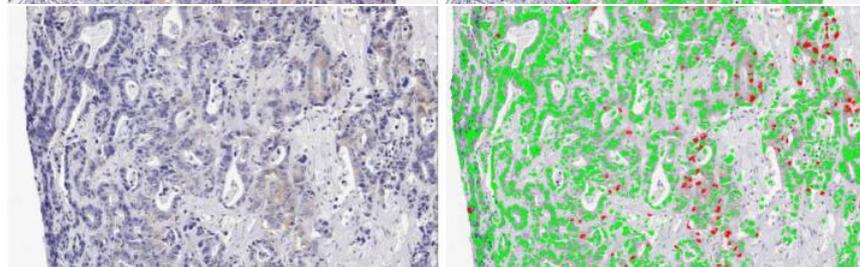
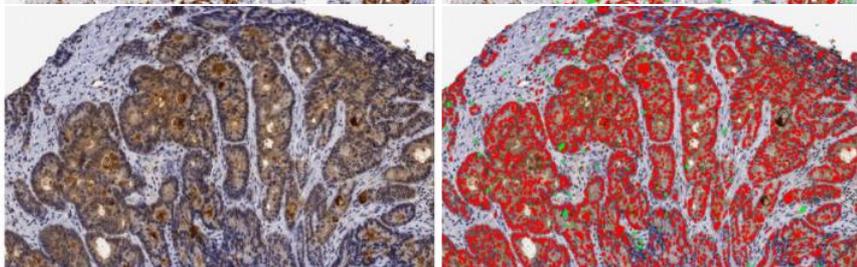
Day 0

Day 14

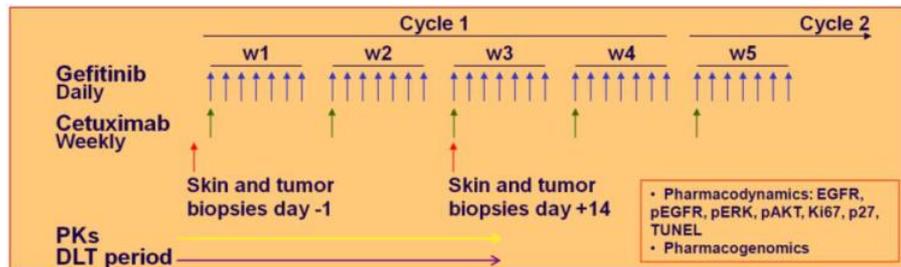
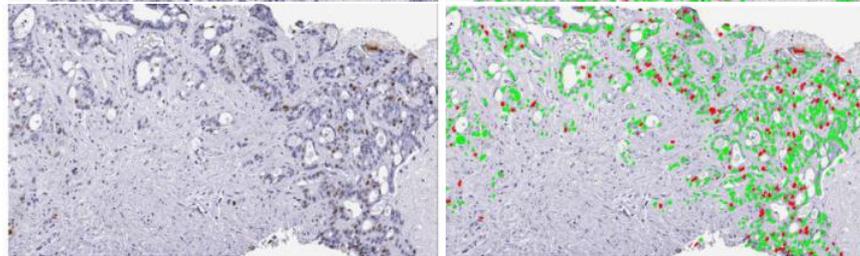
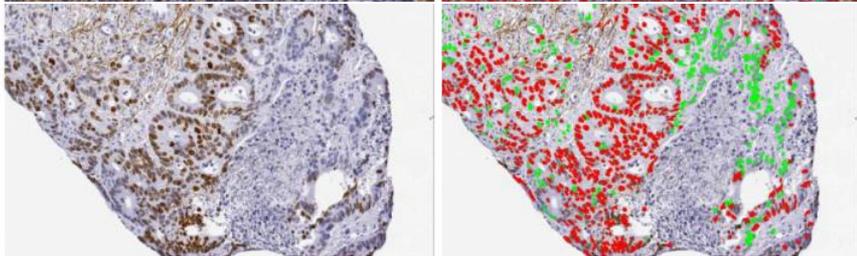
pERK



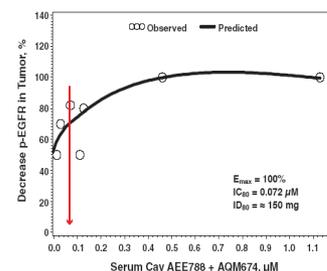
pAKT



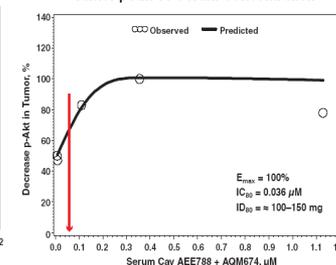
Ki67



Tumor p-EGFR vs Serum Concentration



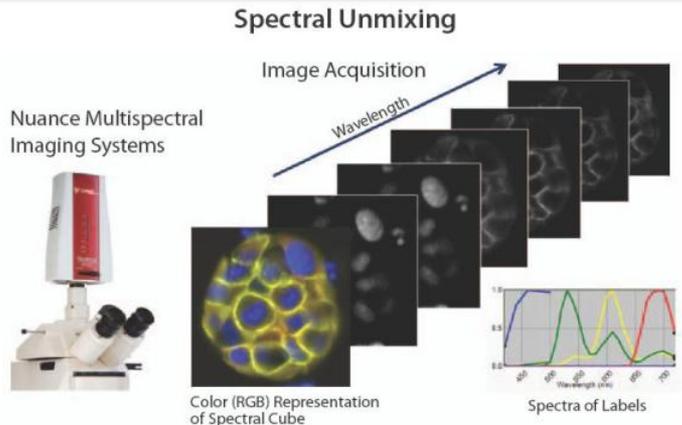
Tumor p-Akt vs Serum Concentration



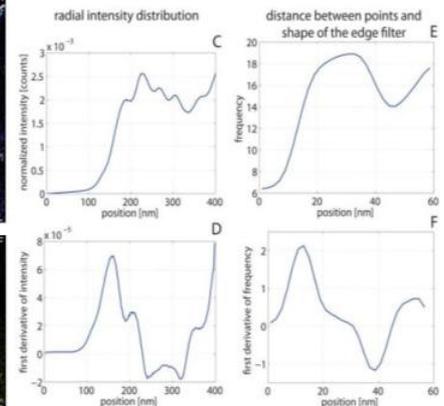
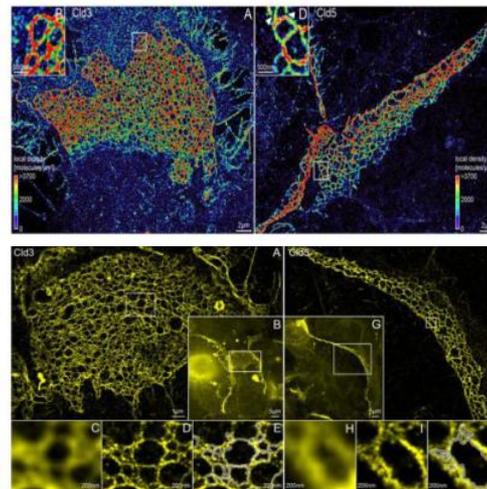
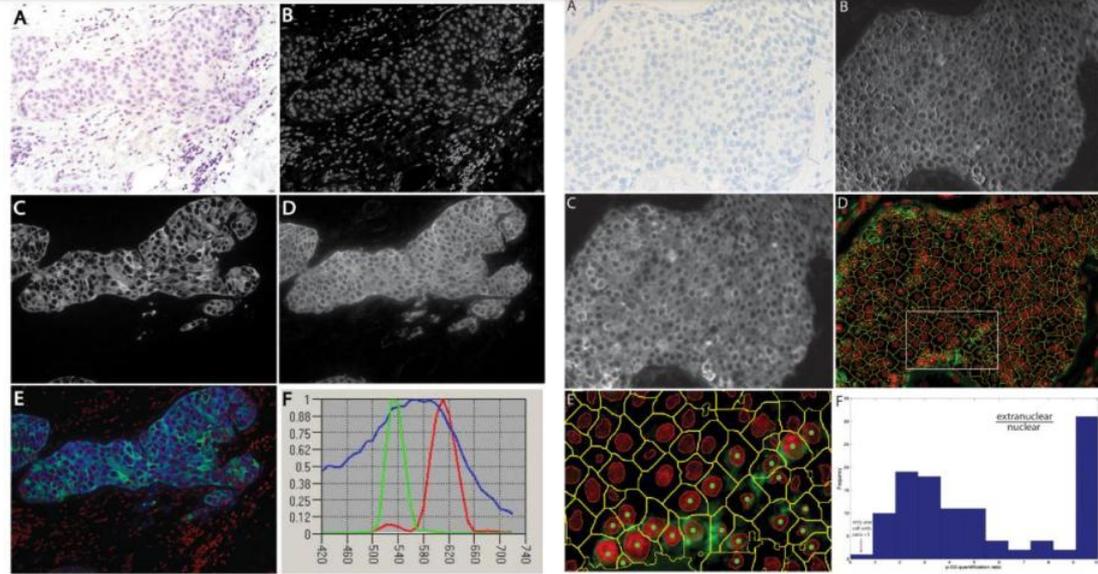
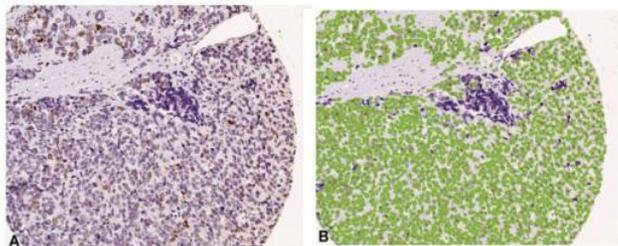
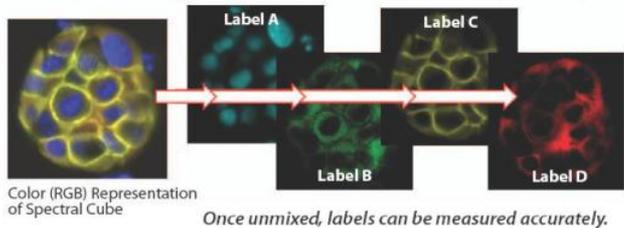
■ Stained cells

■ Non stained cells

Multispectral imaging in automated quantitative scoring

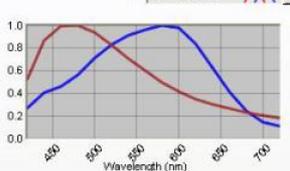


Unmixing of Overlapping Fluorophores using Pure Component Spectra



Library

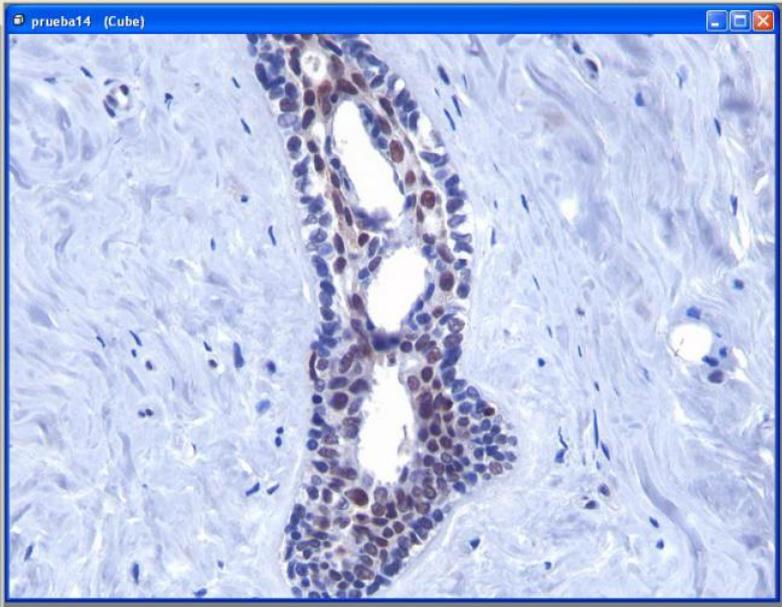
Scaling Normalized



Notes:

Name	Color	Select	Draw
1 C1	Red	<input type="checkbox"/>	
2 C2	Green	<input type="checkbox"/>	
3 Haematox	Blue	<input checked="" type="checkbox"/>	
4 C4	Yellow	<input type="checkbox"/>	
5 C5	Cyan	<input type="checkbox"/>	
6 C6	Magenta	<input type="checkbox"/>	
7 DAB	Brown	<input checked="" type="checkbox"/>	
8 C8	Pink	<input type="checkbox"/>	
9 C9	Black	<input type="checkbox"/>	
10 C10	White	<input type="checkbox"/>	

Restore Defaults Clear All Delete...



Real Component Analysis [RCA]...

Manual Compute Spectra...

Import Spectra From Library...

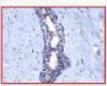
Unmix

CR

Shrink Grow

Thumbnails Measurements Log Cursor

prueba14



Hardware Status Protocol Cursor (X,Y) Average Signal

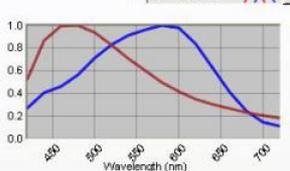
No Hardware

Macros

Run Continue Autobox, Acquire & Unmix Browse...

Library

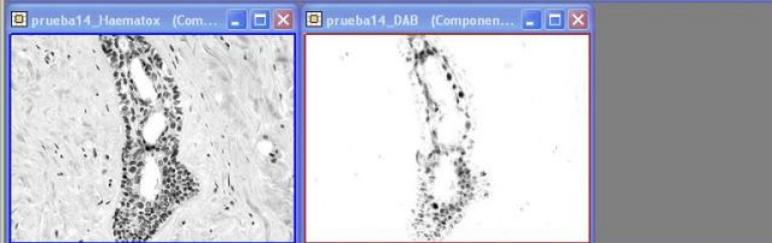
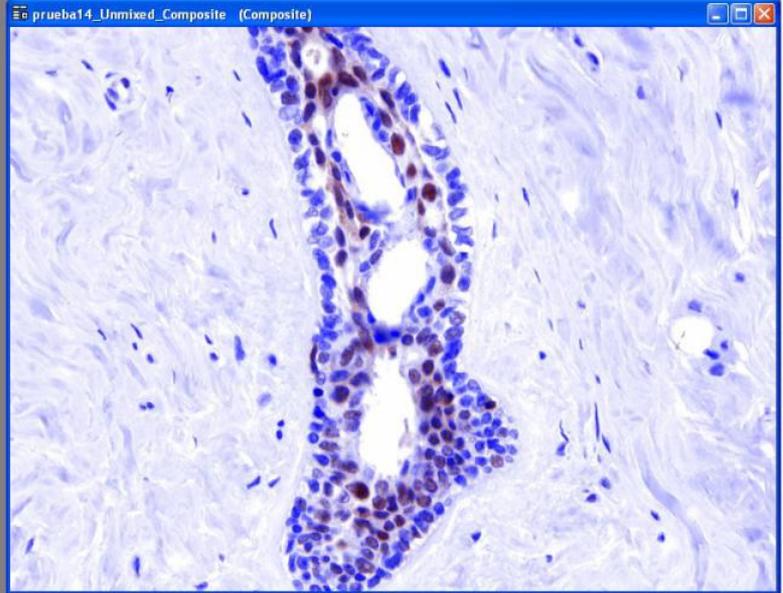
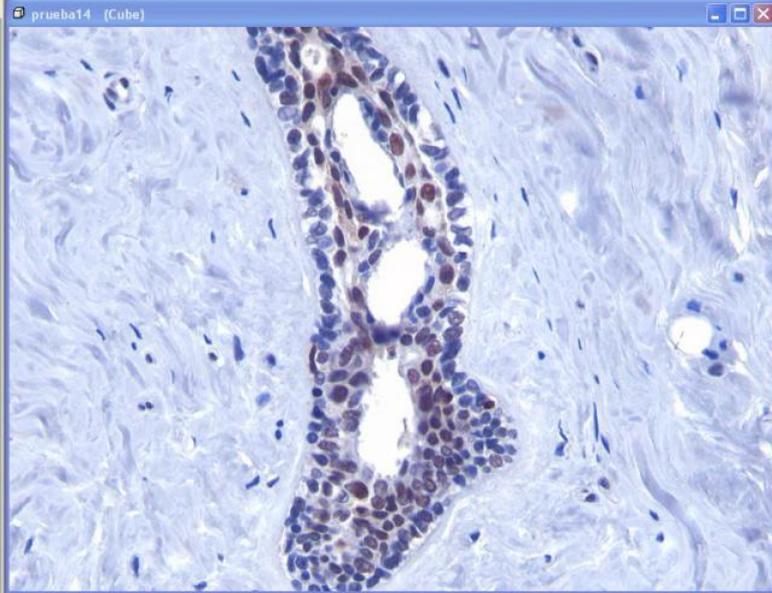
Scaling: Normalized



Notes:

Name	Color	Select	Draw
1 C1	Red	<input type="checkbox"/>	
2 C2	Green	<input type="checkbox"/>	
3 Haematox	Blue	<input checked="" type="checkbox"/>	
4 C4	Yellow	<input type="checkbox"/>	
5 C5	Cyan	<input type="checkbox"/>	
6 C6	Magenta	<input type="checkbox"/>	
7 DAB	Brown	<input checked="" type="checkbox"/>	
8 C8	Pink	<input type="checkbox"/>	
9 C9	Black	<input type="checkbox"/>	
10 C10	White	<input type="checkbox"/>	

Restore Defaults Clear All Delete...



CR

Shrink Grow

Thumbnails Measurements Log Cursor

prueba14 Haematox DAB Composite



Hardware Status Protocol Cursor (X,Y) Average Signal

No Hardware

Macros Run Continue Autoexp, Acquire & Unmix Browse...

Library

Scaling: Normalized

Notes:

Name	Color	SelectDraw
1 C1	Red	<input type="checkbox"/>
2 C2	Green	<input type="checkbox"/>
3 Haematox	Blue	<input checked="" type="checkbox"/>
4 C4	Yellow	<input type="checkbox"/>
5 C5	Cyan	<input type="checkbox"/>
6 C6	Magenta	<input type="checkbox"/>
7 DAB	Brown	<input checked="" type="checkbox"/>
8 C8	Pink	<input type="checkbox"/>
9 C9	Black	<input type="checkbox"/>
10 C10	White	<input type="checkbox"/>

Restore Defaults Clear All Delete...

Real Component Analysis [RCA]...
 Manual Compute Spectra...
 Import Spectra From Library...
 Unmix

Co-localization

Settings: PARP *

Components

Spectral Name	Marker	Color	Visibility
Haematox	Haematox	Blue	<input checked="" type="checkbox"/>
DAB	DAB	Brown	<input checked="" type="checkbox"/>

Thresholding

Marker Name	Minimum Pixels	Mask Color	Visibility
Haematox	20	Blue	<input checked="" type="checkbox"/>
DAB	20	Brown	<input checked="" type="checkbox"/>

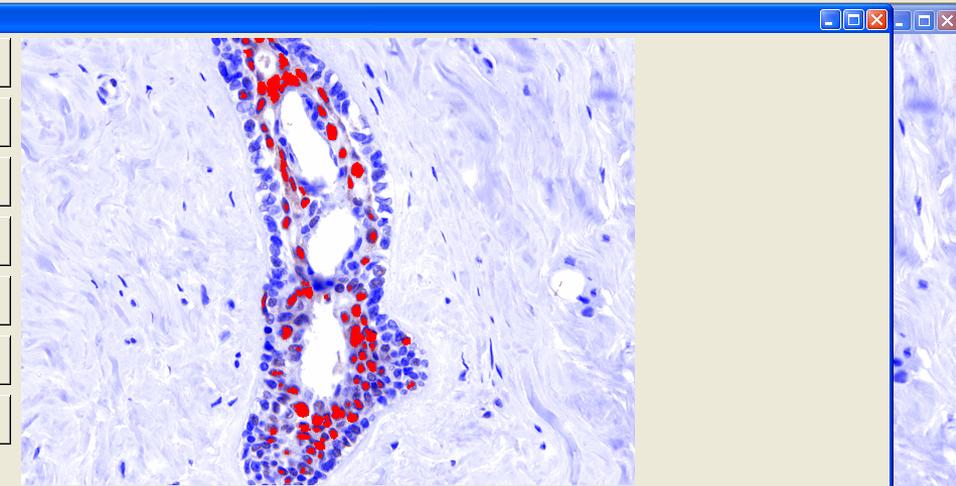
Autothreshold All

Co-localization

Co-loc. Label: Overlap Show Co-loc. Show All Mask Color: Red Visibility:

Markers for Co-localization: Haematox DAB

Denominator (Counterstain): Haematox DAB All Image Pixels



Statistics

	% Co-loc.	% Area: DAB
Percent (%)	1.12%	1.12%

	% Positivity: DAB
Within DAB	--

ROI Number	Marker Area (pixels)	Total Signal (OD)	Avg Signal (OD)	Max Signal (OD)	Standard Deviation (OD)	Area (Pixels)	X Location	Y Location	Major Axis	Minor Axis
DAB Overlap	16149	1369.78	0.0848	0.15	0.015	16149.00	668.00	500.17	1028.16	342.87
DAB Full Image	16149	5053.47	0.00349	0.15	0.0127	1447680.00	694.95	519.54	1392.00	1040.00

Copy Data Export Data Copy Image Export Image Close

Library

Scaling: Normalized

Notes:

Name	Color	Select	Draw
1 C1	Red	<input type="checkbox"/>	
2 C2	Green	<input type="checkbox"/>	
3 Haematox	Blue	<input checked="" type="checkbox"/>	
4 C4	Yellow	<input type="checkbox"/>	
5 C5	Cyan	<input type="checkbox"/>	
6 C6	Magenta	<input type="checkbox"/>	
7 DAB	Brown	<input checked="" type="checkbox"/>	
8 C8	Pink	<input type="checkbox"/>	
9 C9	Black	<input type="checkbox"/>	
10 C10	White	<input type="checkbox"/>	

Restore Defaults Clear All Delete...

Real Component Analysis [RCA]...

Manual Compute Spectra...

Import Spectra From Library...

Unmix

prueba14_Unmixed_Composite (Composite)

Scaling: Preview 0.00

Show Crosshairs

Contrast

Min. Max.
 Clip/Stretch
 Histogram Eq.
 Raw
 Abundance

Enhance Contrast
 Custom

Min Clip: 0.00
 Max Clip: 255.0

Invert Colors

Brightness: 0.00

Threshold: 0 to 0.38

View	Name	Color	Visible	Adjust
<input checked="" type="checkbox"/>	DAB	JetBlack	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	Haematox		<input checked="" type="checkbox"/>	

Display Adjustments

Whole Image
 Single Layer

Composite Coloring Style

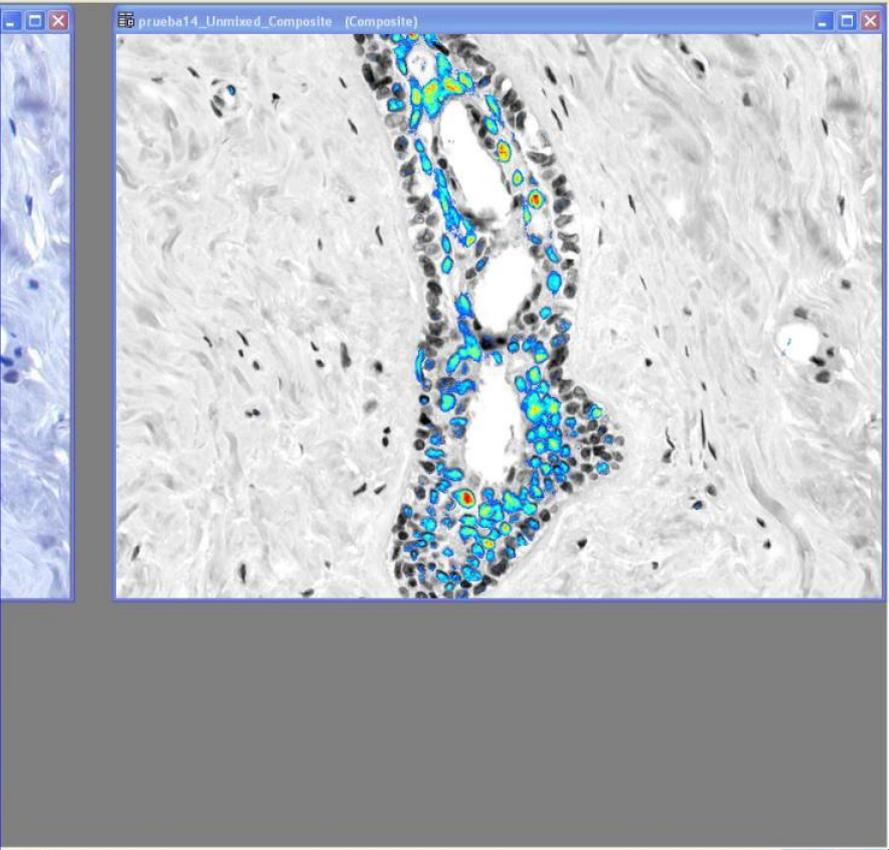
Fluorescence
 Brightfield

Layer Blending Style

Normal (Merged)
 Overlay (Thresholded)

Import Image... Remove Import

Set To Default Close

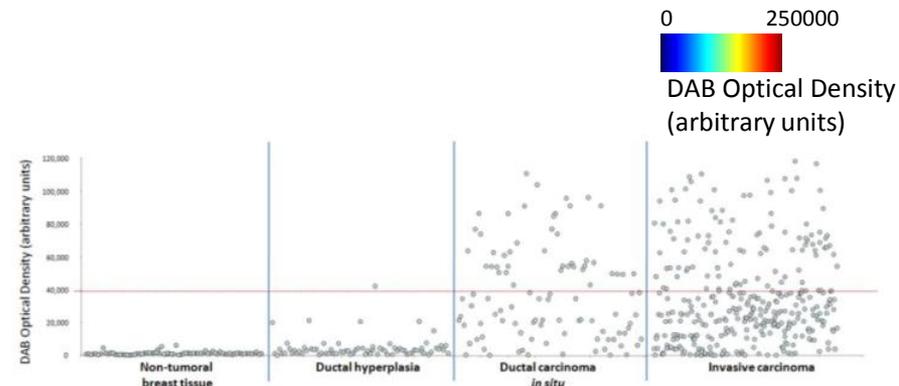
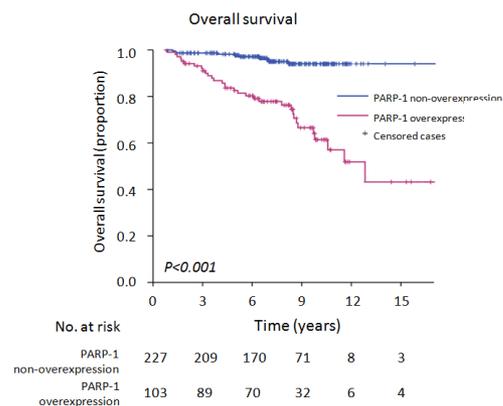
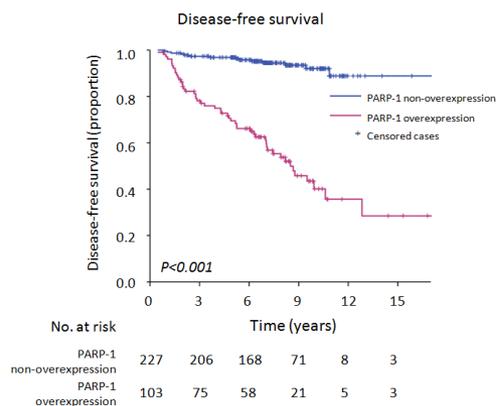
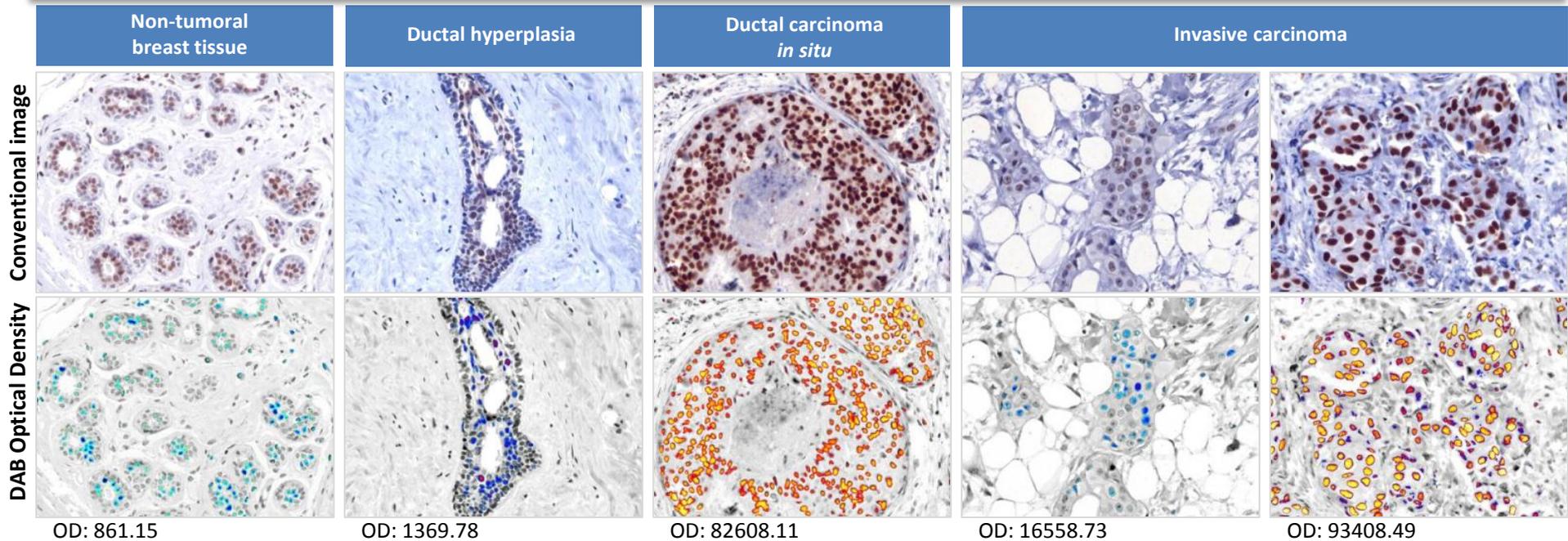


Hardware Status Protocol Cursor (X,Y) Average Signal (00)

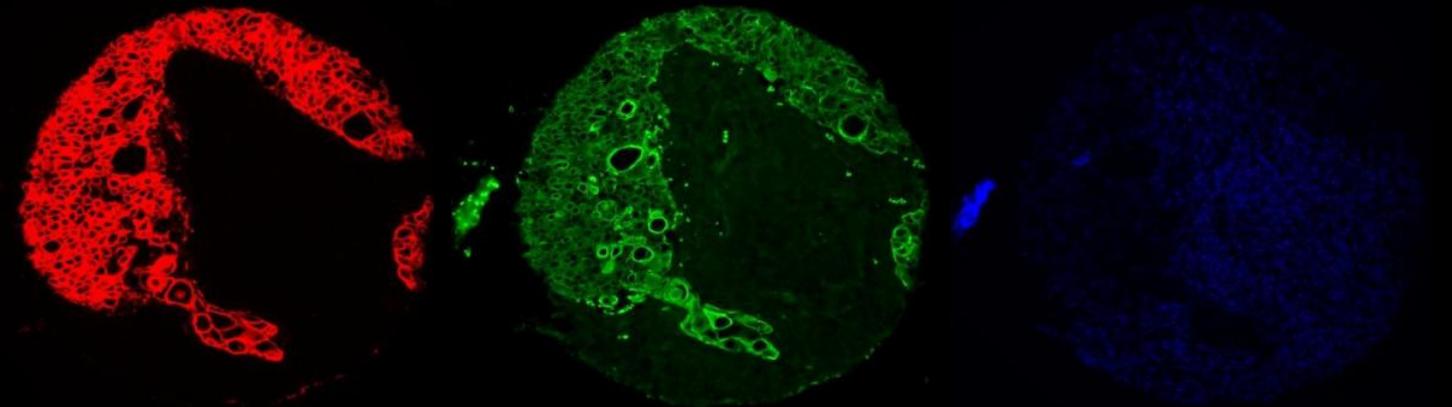
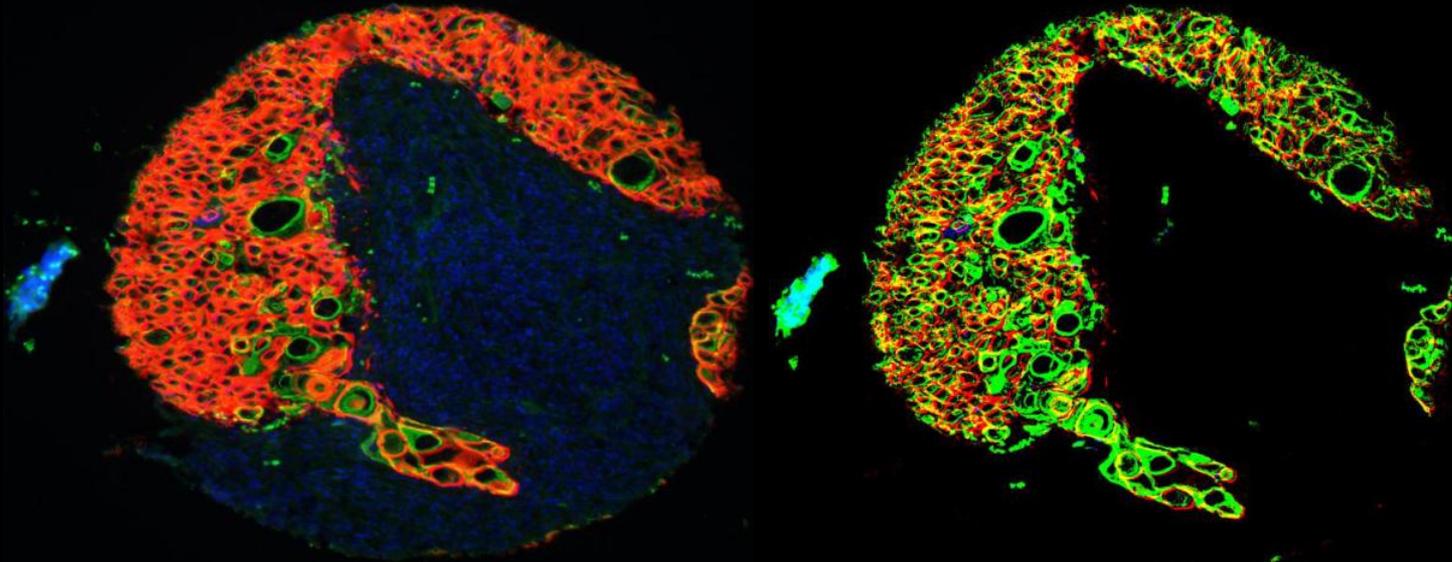
Co-localiz...

Macros: Run Continue Autoexp, Acquire & Unmix

Multispectral imaging in automated quantitative scoring



Multispectral imaging in automated quantitative scoring: the AQUA platform

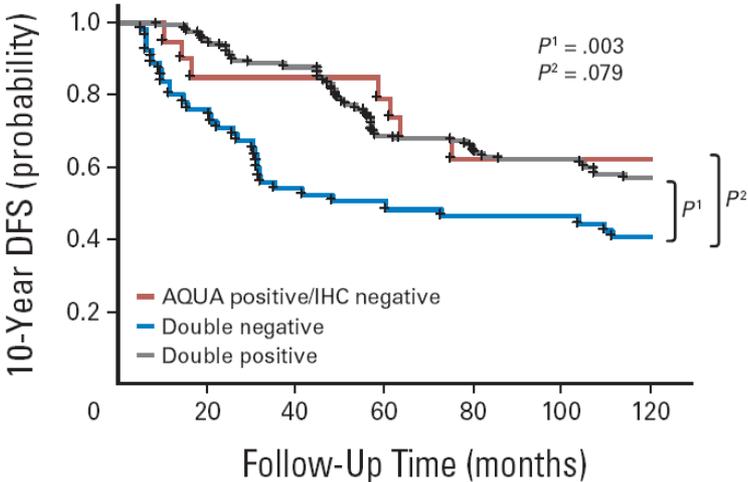
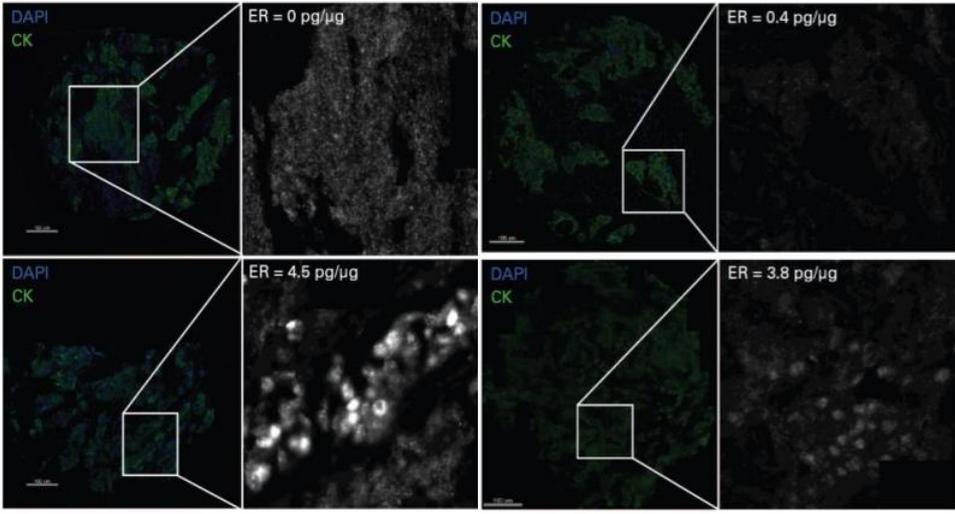
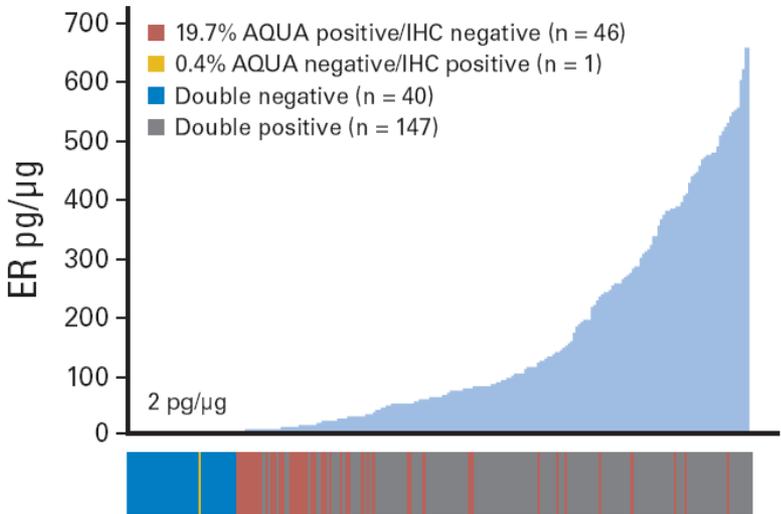


HER2

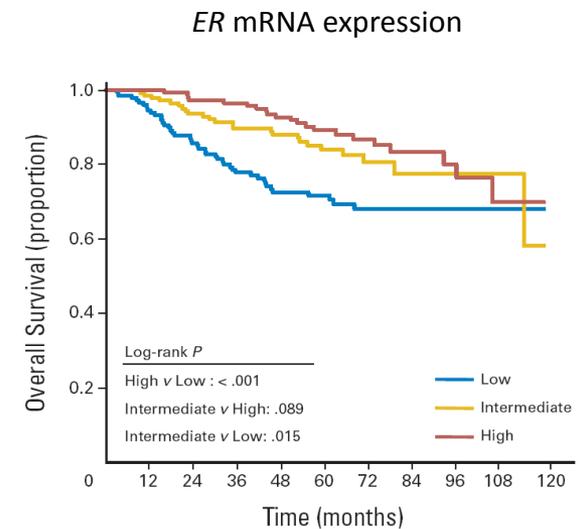
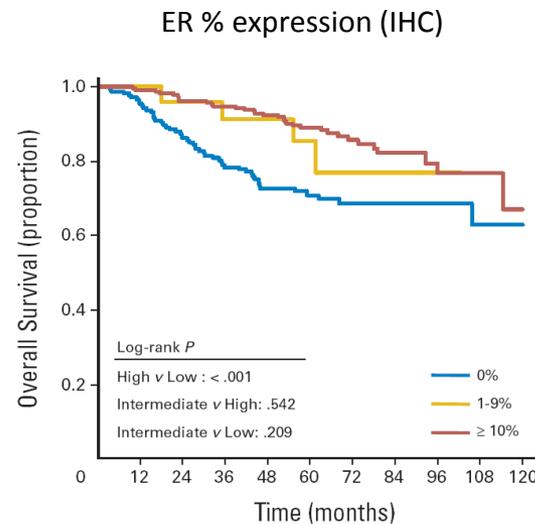
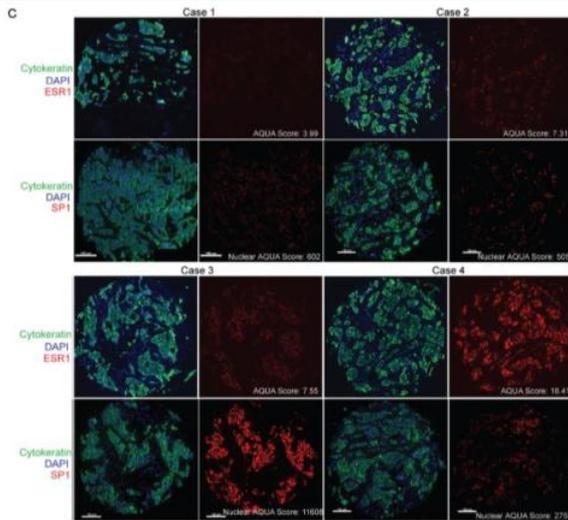
CK

DAPI

Impact of false negative results in estrogen receptor measurement in breast cancer due to IHC assay sensitivity



Estrogen receptor mRNA expression in breast cancer: correlation with response to tamoxifen

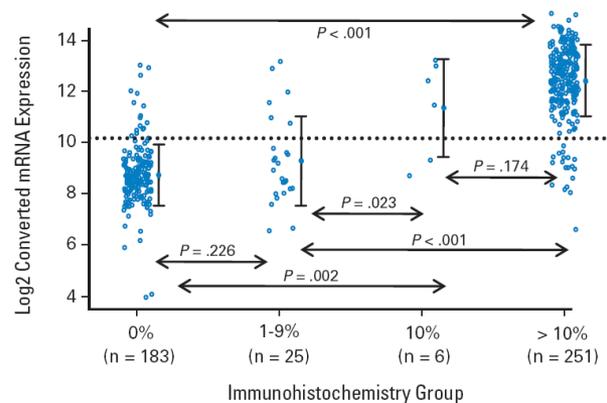


No. at risk

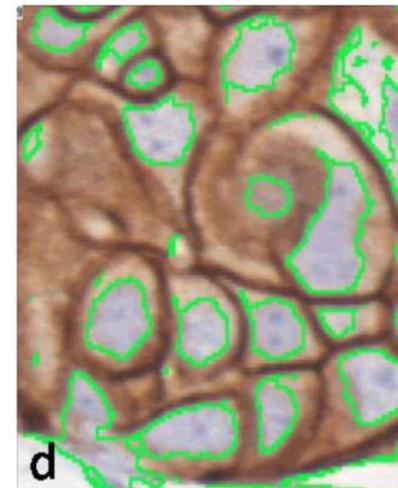
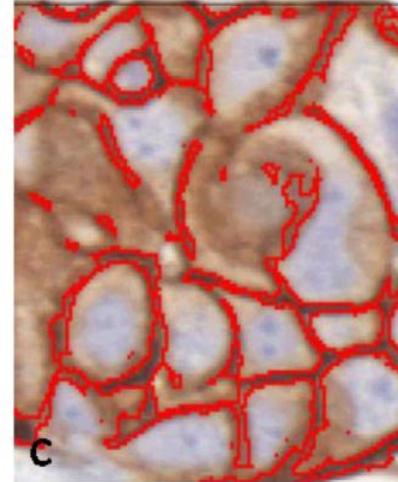
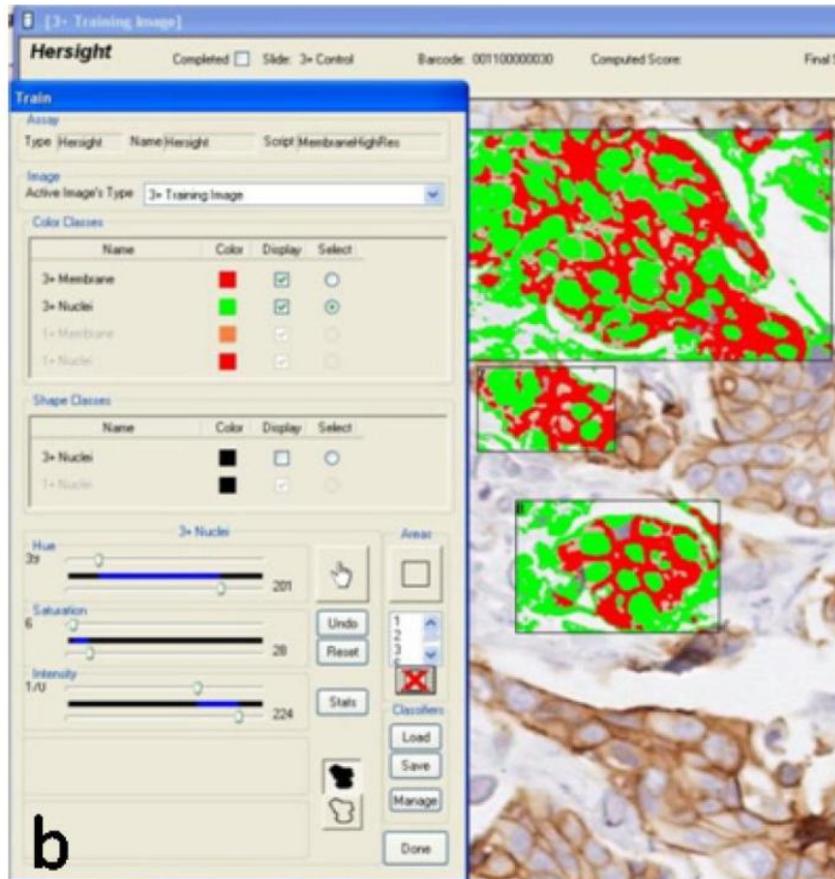
0%	179	168	147	128	107	75	47	29	17	10	4
1-9%	24	24	22	20	20	10	7	2	1		
≥ 10%	243	237	226	206	182	134	87	49	28	14	4

No. at risk

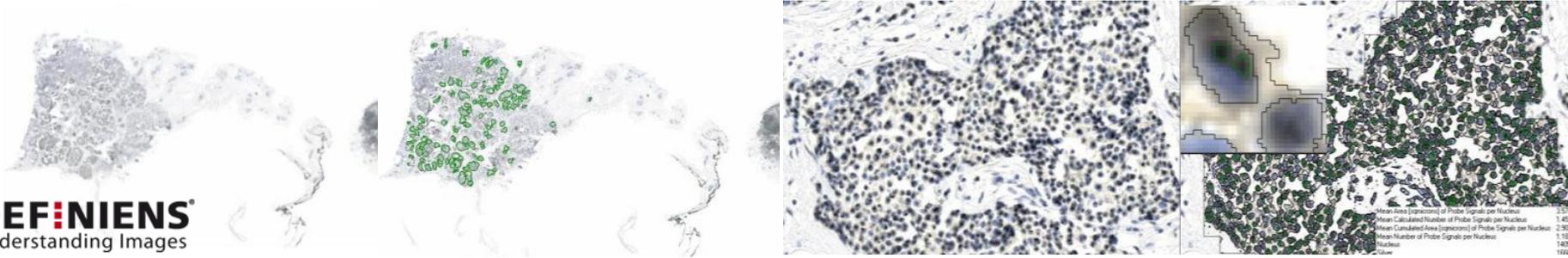
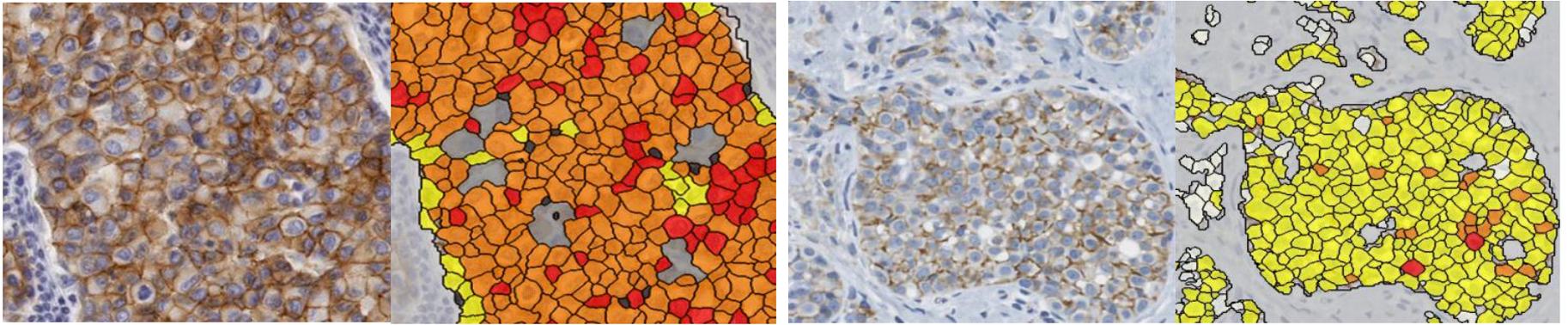
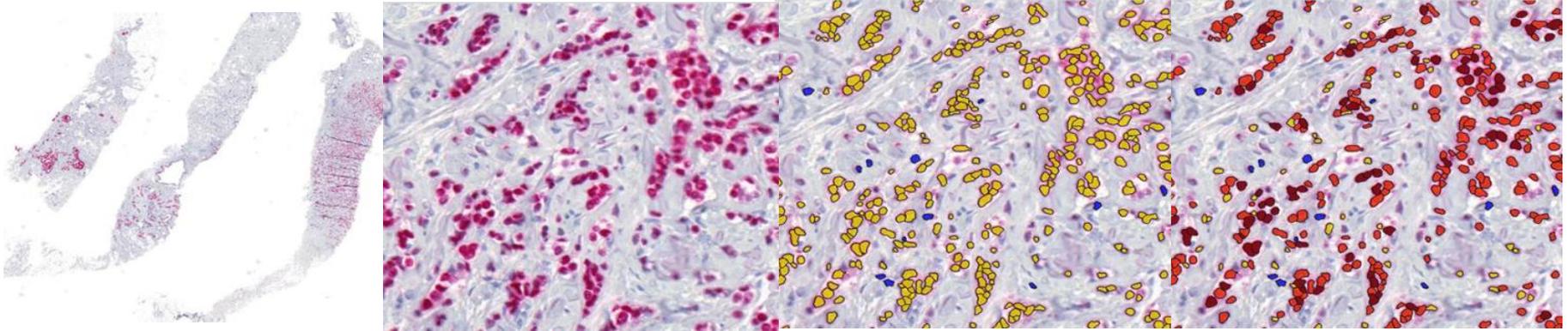
Low	149	140	123	107	93	66	42	25	14	10	4
Intermediate	149	143	130	114	99	71	41	18	10	5	2
High	148	146	142	133	117	82	58	37	22	9	2



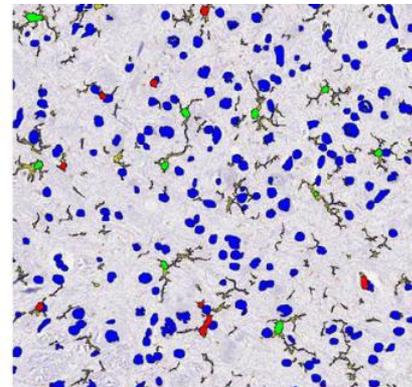
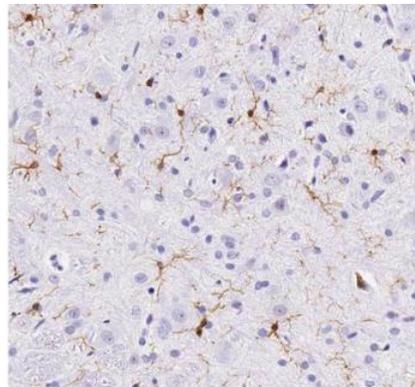
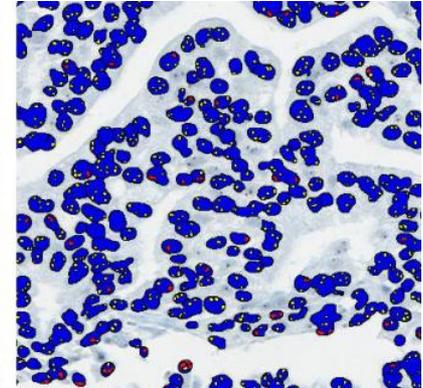
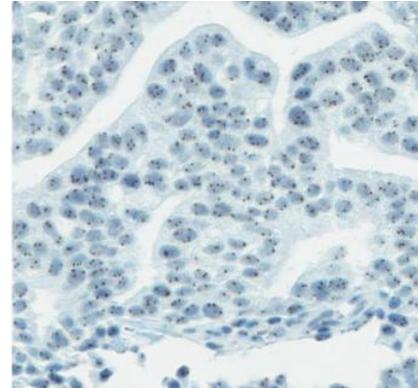
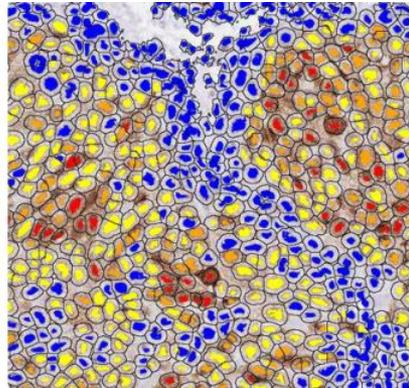
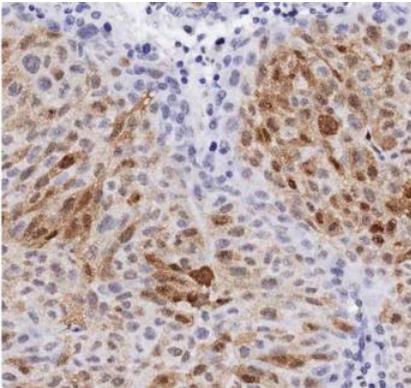
Ariol (Applied Imaging) HER2 scoring in breast cancer



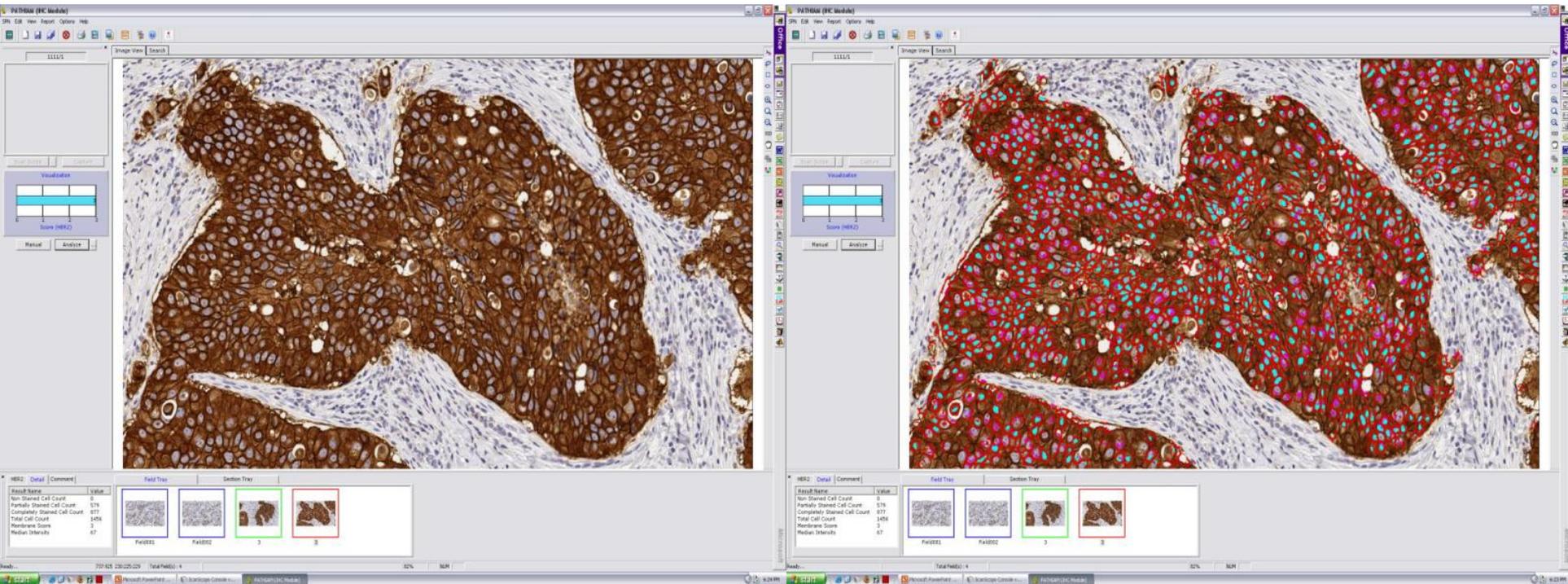
Definiens ER and HER2 scoring in breast cancer



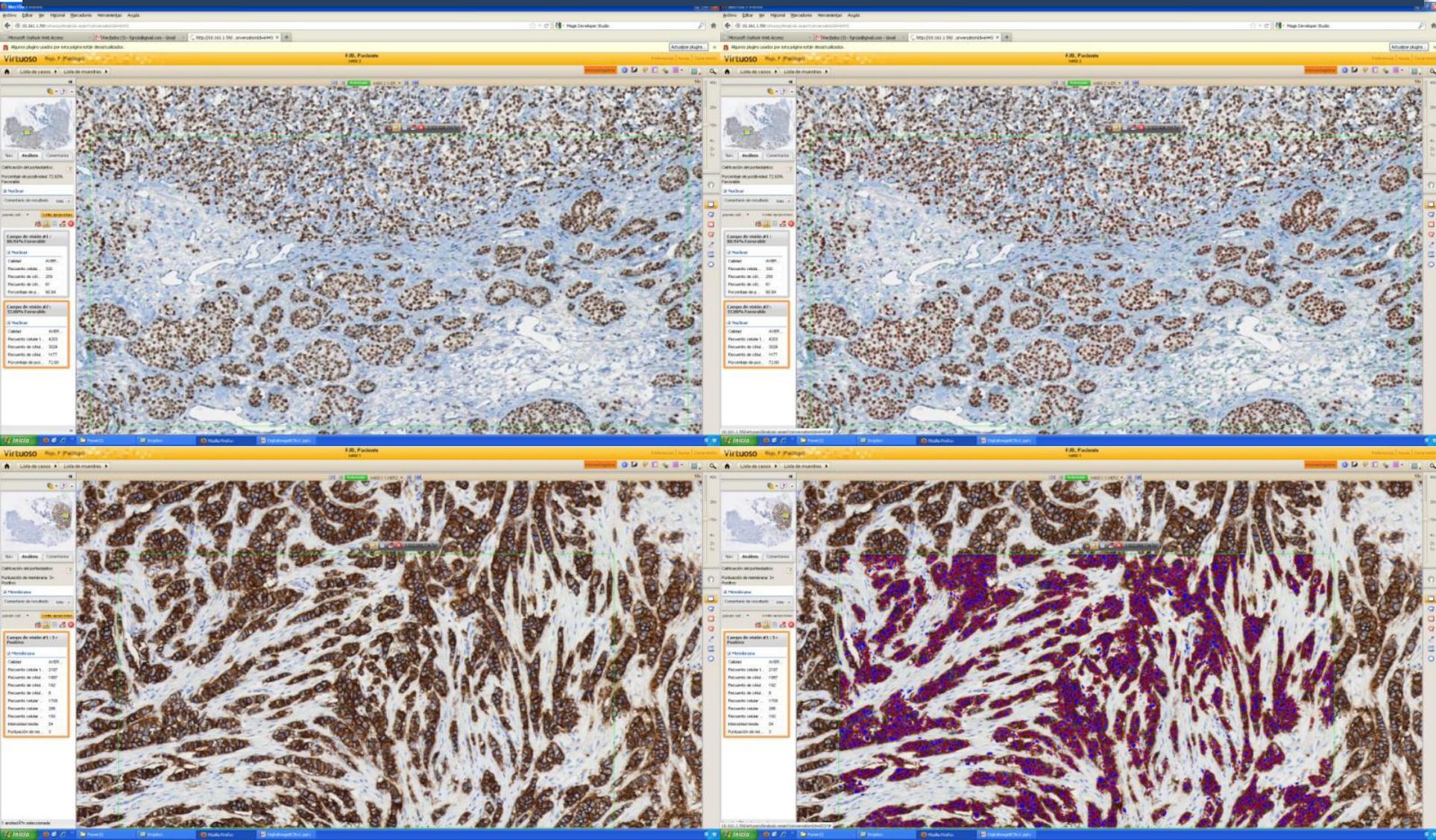
Precision (Aperio) ER and HER2 scoring in breast cancer



Pathiam HER2 scoring in breast cancer



Virtuoso ER and HER2 scoring in breast cancer



Final remarks: Pros and cons

- Morphology-driven integration of new approaches and generation of knowledge: increased technological innovation and biological information
- Evolution along Radiology/Imaging lines: market & technology forces start trend to digital imaging and significant workload & throughput implications
- Clinical demand: quantitative (qualitative becoming quantitative), relational data and individualized risk assessment:
 - greater concern with analytical precision,
 - reproducibility,
 - accuracy,
 - specificity,
 - reliability
 - “stains” becoming “assays”
 - results directly tied to treatment, not just prognosis
- Images must be free from artifacts
- Systems may be discrepant when tumor cells have low levels of staining
- Interfering non-specific staining within selected areas
- Small amounts of stained tissue can erroneously generate lower scores
- Expense of CAIA may be hard to justify where volumes are low
- Image analysis frequently requires interactive input by the pathologist: Increased time requirements
- Learning algorithms: systems that improve with experience following pathologist feedback
- Whole slide imaging (WSI) to eliminate the need to standardize different systems, automatic ROI selection and image analysis
- Shortened analysis time
- To improve workflow: adopt virtual workflow-centric systems feasible for routine practice (that may potentially show better results)
- AP-LIS and CAIA system integration
- Clinical outcome studies are needed