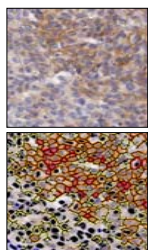


Background

Reliable image analysis requires consistent slide scanning. Aperio's ScanScope® systems provide an automatic calibration each time a slide is scanned that compensates for the current light and optical variations, superior to factory or daily calibration. Aperio's IHC HER2 Image Analysis algorithm provides the HER2 score and the percentages of detected and classified cells allowing the measurement of any variation with high precision. A suite of precision studies using 8 HER2 slides were conducted to measure the variations introduced by the systems, operators and pathologists.

IHC HER2 Image Analysis



HER2 Score: 3+

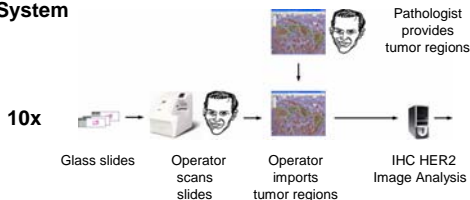
3+ Cells:	11.0%
2+ Cells:	35.7%
1+ Cells:	51.4%
0 Cells:	1.9%

Data

8 HER2 slides with 2 slides per HER2 score 0, 1+, 2+ and 3+ were used for all studies. The HER2 scores were assessed by 3 pathologists (P1, P2, P3) using manual microscopy.

	P1, P2, P3	P1, P2, P3
#1	0, 0, 0	#2 0, 0, 1+
#3	0, 1+, 1+	#4 1+, 1+, 0
#5	2+, 2+, 2+	#6 2+, 2+, 2+
#7	3+, 3+, 3+	#8 3+, 3+, 3+

1) Intra-System



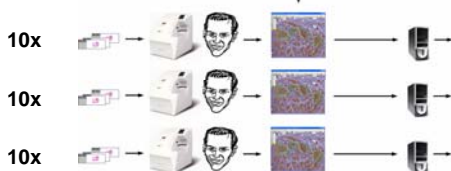
HER2 Score	Cumulated Percentages			
	PA	Avg SD	Max SD	Avg Range
100%	0.69%	2.46%	1.22%	7.14%

2) Intra-System / Inter-Day



100%	0.67%	2.43%	1.68%	12.07%
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3) Inter-Systems



100%	0.69%	2.46%	1.22%	7.14%
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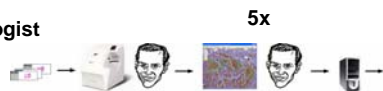
100%	0.73%	1.65%	1.28%	5.09%
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100%	0.70%	1.34%	1.28%	4.70%
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Combined

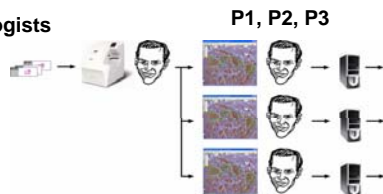
100%	0.78%	2.41%	1.28%	8.95%
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4) Intra-Pathologist



90%	2.44%	8.08%	3.51%	18.61%
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5) Inter-Pathologists



83%	9.77%	27.09%	11.20%	48.26%
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Design

ScanScope and Operator Precision

- The glass slides were scanned 10 times on the same ScanScope system.
- The glass slides were scanned 20 times on the same ScanScope system on different days.
- The glass slides were scanned 10 times on 3 different ScanScope systems. To eliminate the variations introduced by the pathologists, the same tumor regions (provided by a pathologist) were used for the image analysis in studies 1 – 3.

Pathologist Precision

The system variations were put into perspective by assessing the variations introduced by pathologists as a result of outlining different tumor regions.

- The same pathologist provided the tumor regions for the image analysis 5 times at different moments in time.
- Three different pathologists provided the tumor regions for the image analysis. To eliminate the variations introduced by the system and the operator, the same digital slides (no rescanning) were used in studies 4 – 5.

Result

The statistical analysis evaluated the Percent Agreement (PA) for the HER2 score, and the average and maximum Standard Deviation (SD) and range (max - min) for the cumulative percentages (percentage of 3+ cells, percentage of 3+ and 2+ cells, and percentage of 3+, 2+ and 1+ cells) on which the HER2 scoring scheme is based.

The ScanScope systems demonstrated a perfect PA of 100% for the HER2 scores with extremely small average SD (< 1%) and range (< 2%) for the cumulative percentages. No inter-operator variability was observed.

The ScanScope systems variations were insignificant compared to the variations introduced by the pathologists due to choosing the tumor regions for image analysis.

Conclusion

Aperio's ScanScope systems provide excellent reproducibility from scan to scan and from instrument to instrument.