

# LEICA BIOSYSTEMS WHITE PAPER

## APERIO GT 450 IMPROVES THROUGHPUT BY 64% AND REDUCES QC TECH TIME BY 94% IN WORKFLOW STUDY

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### Background

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NeoGenomics is a large research and reference laboratory located in California and has experienced significant increases in annual slide volumes. The NeoGenomics senior management team was tasked with evaluating ways to scale up digital pathology operations to keep up with increasing demand. Consequently, the laboratory director desired to perform a comparative research study to assess the performance of the Aperio GT 450 versus Aperio AT2. Throughput, QC tech time and other performance metrics were measured.

## Methodology

### Samples

A total of 155 slides, that were representative samples from the high volume reference laboratory, were part of this study. Samples included:

- 35 individual H&E stained slides
- 36 breast IHC slides evaluated for key biomarkers along with 10 associated breast H&E slides
- 26 colon IHC stained slides for key biomarkers along with 8 associated colon H&E slides
- 33 squamous mucosa CISH stained slides for HPV biomarkers (RNA ISH) along with 7 associated H&E slides

### H&E stained slides

35 Individual H&E stained slides included in the study

Organ	Method	# of slides
Brain	H&E	1
Cervix	H&E	2
Gall bladder	H&E	1
Lung	H&E	4
Prostate	H&E	20
Right iliac bone	H&E	1
Soft palate	H&E	1
Stomach	H&E	3
Tongue	H&E	1
Uterus	H&E	1
<b>Total</b>		<b>35</b>

### IHC breast biomarkers

36 breast IHC slides evaluated for key biomarkers along with 10 associated breast H&E slides were included in the study.

Organ	Method	Stain	# of slides	Case #
Breast	IHC/H&E	HER2, ER, PR, Ki67, H&E	5	1
Breast	IHC/H&E	HER2, ER, PR, Ki67, p53, H&E	5	2
Breast	IHC/H&E	ER, PR, Ki67, p53, H&E	5	3
Breast	IHC/H&E	ER, PR, Ki67, p53, H&E	5	4
Breast	IHC/H&E	ER, PR, Ki67, p53, H&E	5	5
Breast	IHC/H&E	HER2, ER, PR, Ki67, H&E	5	6
Breast	IHC/H&E	HER2, PR, Ki67, H&E	4	7
Breast	IHC/H&E	HER2, Ki67, p53, H&E	4	8
Breast	IHC/H&E	HER2, Ki67, p53, H&E	4	9
Breast	IHC/H&E	HER2, Ki67, p53, H&E	4	10
		<b>Total slides</b>	<b>46</b>	

**Colon biomarkers**

26 colon IHC stained slides evaluated for key biomarkers along with 8 associated colon H&E slides were included in the study.

<b>Organ</b>	<b>Method</b>	<b>Stain</b>	<b># of slides</b>	<b>Case #</b>
Colon	IHC/H&E	MLH-1, MSH-2, MSH-6, PMS-2, H&E	5	1
Colon	IHC/H&E	MLH-1, MSH-2, MSH-6, PMS-2, H&E	5	2
Colon	IHC/H&E	MLH-1, MSH-2, MSH-6, PMS-2, H&E	5	3
Colon	IHC/H&E	MLH-1, MSH-2, MSH-6, PMS-2, H&E	5	4
Colon	IHC/H&E	MLH-1, MSH-2, MSH-6, PMS-2, H&E	5	5
Colon	IHC/H&E	MSH-2, MSH-6, H&E	3	6
Colon	IHC/H&E	MLH-1, PMS-2, H&E	3	7
Colon	IHC/H&E	MLH-1, PMS-2, H&E	3	8
		<b>Total slides</b>	<b>34</b>	

**Squamous mucosa RNA ISH biomarkers**

33 squamous mucosa CISH stained slides evaluated for HPV biomarkers (RNA ISH) along with 7 associated H&E slides were included in the study.

<b>Organ</b>	<b>Method</b>	<b>Stain</b>	<b># of slides</b>	<b>Case #</b>
Squamous Mucosa	CISH/H&E	HPV 16/18, HR 18, HPV LR10, HPV RNA-, HPV RNA+, HPV H&E	6	1
Squamous Mucosa	CISH/H&E	HPV 16/18, HR 18, HPV LR10, HPV RNA-, HPV RNA+, HPV H&E	6	2
Squamous Mucosa	CISH/H&E	HPV 16/18, HR 18, HPV LR10, HPV RNA-, HPV RNA+, HPV H&E	6	3
Squamous Mucosa	CISH/H&E	HPV 16/18, HR 18, HPV LR10, HPV RNA-, HPV RNA+, HPV, H&E	6	4
Squamous Mucosa	CISH/H&E	HPV 16/18, HR 18, HPV LR10, HPV RNA-, HPV RNA+, HPV, H&E	6	5
Squamous Mucosa	CISH/H&E	HPV 16/18, HR 18, HPV RNA-, HPV RNA+, HPV H&E	5	6
Squamous Mucosa	CISH/H&E	HPV 16/18, HR 18, HPV RNA-, HPV RNA+, HPV H&E	5	7
		<b>Total slides</b>	<b>40</b>	

## Equipment

Equipment Type / Description	Identification / Serial Number
Aperio GT 450 next generation scanner	Serial number 12001 with hardware version 1.0.1 and controller version 1.0.0.5055
Dell R740XL DSR server loaded with Aperio eSlide Manager and Aperio ImageScope Version 12.4.	Aperio eSlide Manager Version 12.4.2.5010
Dell 5820 workstation with ImageScope version 12.4, Win 10 operating system and ICC calibration file loaded on workstation, Dell 24 inch calibrated monitor model.	Aperio ImageScope Version 12.4.2.5010 ICC calibration file version Aperio GT 450
Scanner Admin Manager (SAM) server Dell R640	Serial number SAMBAR2
Scanner Admin Manager (SAM) client software	Version 1.0.0.5052
Aperio AT2 scanner	Serial number 7553 with hardware version 102.0.7.5 and controller version 102.0.4.201

## Workflow Steps Start and End Points

Starting point: flats loaded with the 155 slides with ethanol

AT2	Step	Workflow Steps	Timing Category
	1	Clean all slides	Hands-on time
	2	Insert all slides into Aperio AT2 racks per user manual instructions	Hands-on time
	3	Load all racks into Aperio AT2	Hands-on time
	4	Pre-snaps	Scan time
	5	Manually adjust scan area (green box)	Hands-on time/ QC Tech time
	6	Manually adjust or add focus points	Hands-on time/ QC Tech time
	7	Scan all slides at 20x	Scan time
	8	Review image quality in 5 image points for each image created	Hands-on time/ QC Tech time
	9	Remove racks and place on lab bench	Hands-on time
	10	Put slides back in flats	Hands-on time

<b>GT 450</b>	<b>Step</b>	<b>Workflow Steps</b>	<b>Timing Category</b>
	1	Clean all slides	Hands-on time
	2	Insert all slides into Aperio GT 450 racks per user manual instructions	Hands-on time
	3	Continuously load all racks into Aperio GT 450 while automatic scanning occurs	Hands-on time/ Scan time
	4	Review tissue finder results via macro image	Hands-on time/ QC Tech time
	5	Remove racks and place on lab bench	Hands-on time
	6	Put slides back in flats	Hands-on time

## Study Endpoint Measurements

### Definitions:

#### » QC tech time

- Aggregate time the operator spent with the instrument that was required for slide quality or slide inspection purposes, measured in hours, minutes and seconds.

#### » Hands on time

- Aggregate time a tech spent performing the workflow steps from beginning to end. This included steps 1, 2, 3, 4, 5, 6, 8, 9 and 10 for the Aperio AT2 (see table of workflow steps below)

and steps 1, 2, 4, 5 and 6 for the Aperio GT 450 (see table of workflow steps below). Each measured in hours, minutes and seconds.

#### » Turnaround time (TAT)

- Total amount of time to perform the workflow steps from beginning to end measured in hours, minutes and seconds.

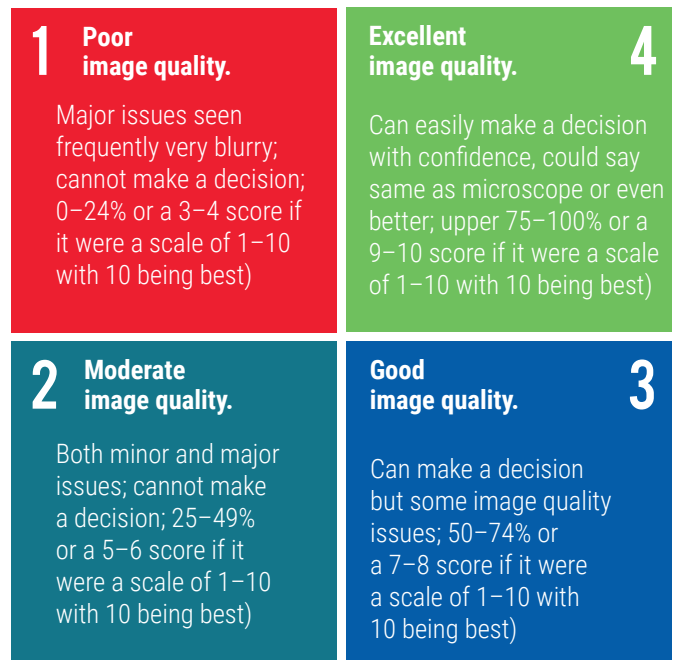
#### » Slide throughput

- Number of slides processed for all workflow steps beginning to end measured in slides per hour.

## Image Quality

Each of the three participating pathologists viewed and scored image quality for 155 images from the sample set generated with the Aperio AT2, and 155 images from the sample set generated with the Aperio GT 450. Images were viewed on the Aperio Viewing Station running Aperio eSlide Manager 12.4 Image Management Software, and Aperio ImageScope 12.4 Viewing Software.

There was a minimum of a 2 week wash out period between the reads on images generated from Aperio AT2 and Aperio GT 450. Image quality was assessed by each participating Pathologist using a quadrant-based scoring criteria, as shown in Figure 1. For example, a score of 4 was recorded by the pathologist if he or she assessed that the image quality fit with the description in quadrant 4.



**Figure 1 (above):** Quadrant-based scoring system that is used by Pathologists to score image quality during image quality testing at Leica Biosystems.

## Results

### Total tech QC time

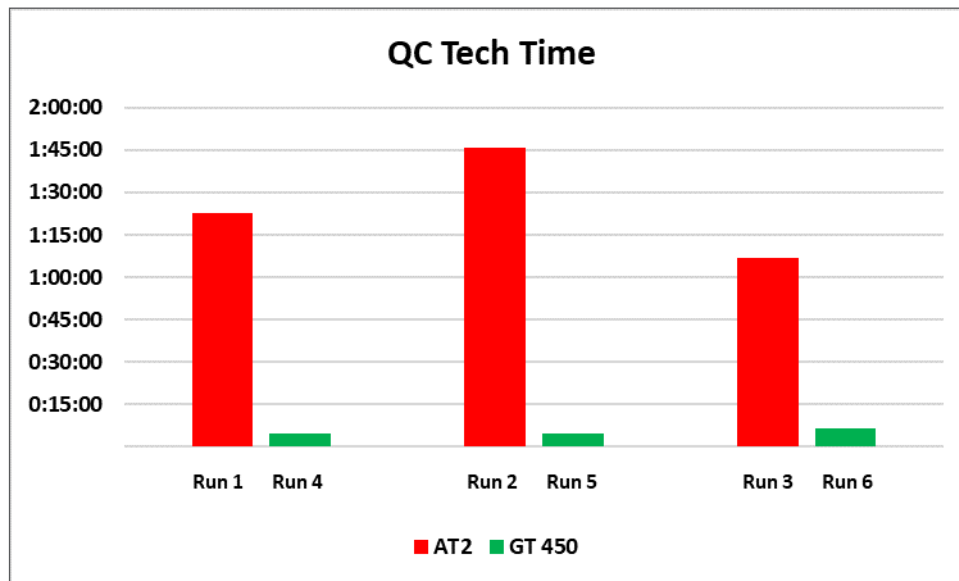
94% reduction.

QC tech time is defined as the aggregate time the operator spent with the instrument. This is the time that

was required for slide quality or slide inspection purposes and is a subset of the total hands-on time.

Table 1 (below): Average Tech QC time was reduced from about 1 hour and 25 minutes to only 5 minutes with Aperio GT 450. This is a 94% reduction in Tech QC time.

<b>AT2</b>	<b>Run 1</b>	<b>Run 2</b>	<b>Run 3</b>	<b>Avg</b>
Tech QC Time (h:mm:ss)	1:22:38	1:45:41	1:06:46	1:25:02
<b>GT 450</b>	<b>Run 4</b>	<b>Run 5</b>	<b>Run 6</b>	<b>Avg</b>
Tech QC Time (h:mm:ss)	0:04:54	0:04:38	0:06:43	0:05:25



**Figure 2 (above):** QC tech time for Aperio AT2 and Aperio GT 450 by run

**Total hands-on time**

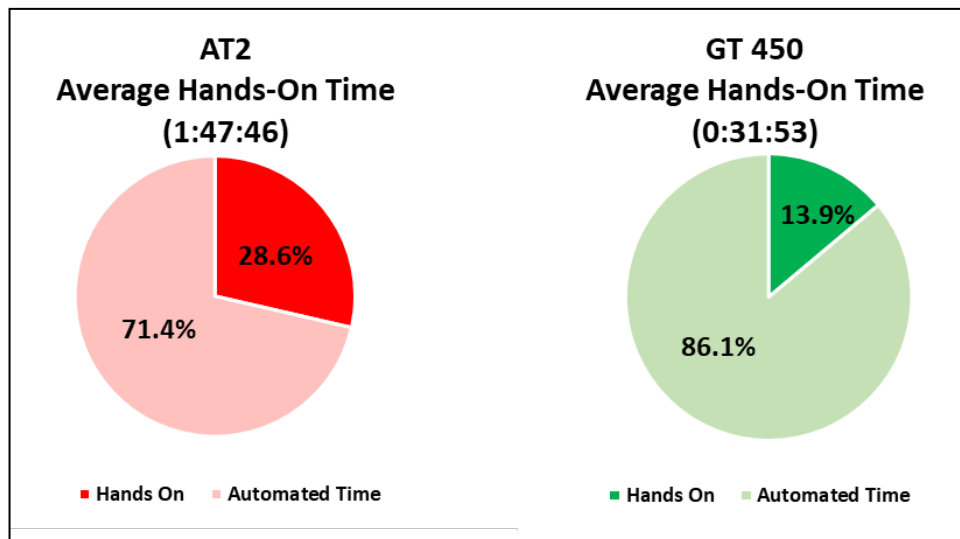
70% reduction.

The “hands-on time,” defined as any tech interaction with the instrument, was recorded for each of the runs.

Table 2 (below): Total hands on time summary.

The Aperio AT2 required a significant amount of tech interaction (average of 1 hour, 47 minutes, 46 seconds) to complete the 155 slide run. Conversely, the Aperio GT 450 showed an average hands-on time of just 31 minutes, 53 seconds, which is less than one-third of the time of the Aperio AT2. Note: hands on time includes slide cleaning and loading slides into racks.

Total Hands-On Time Summary	AT2 (20x)				GT 450 (40x)			
	Run 1	Run 2	Run 3	Avg	Run 1	Run 2	Run 3	Avg
Hands-on	1:42:27	2:14:42	1:26:10	1:47:46	0:34:42	0:33:08	0:27:49	0:31:53
Hands-on sec	6147	8082	5170	6466	2082	1988	1669	1913
Tech QC Time (h:mm:ss)	6:03:42	6:50:17	5:56:40	6:16:53	3:56:25	3:50:49	3:40:30	3:49:15
Tech QC Time (h:mm:ss)	6147	24617	21400	22613	14185	13849	13230	13755
% Total	28.2%	32.8%	24.2%	28.6%	14.7%	14.4%	12.6%	13.9%



**Figure 3 (above):** Overall, the average hands-on time consumed nearly 29% of the total time for the Aperio AT2 runs, whereas the Aperio GT 450 required only 14% of the total time.



**Throughput**

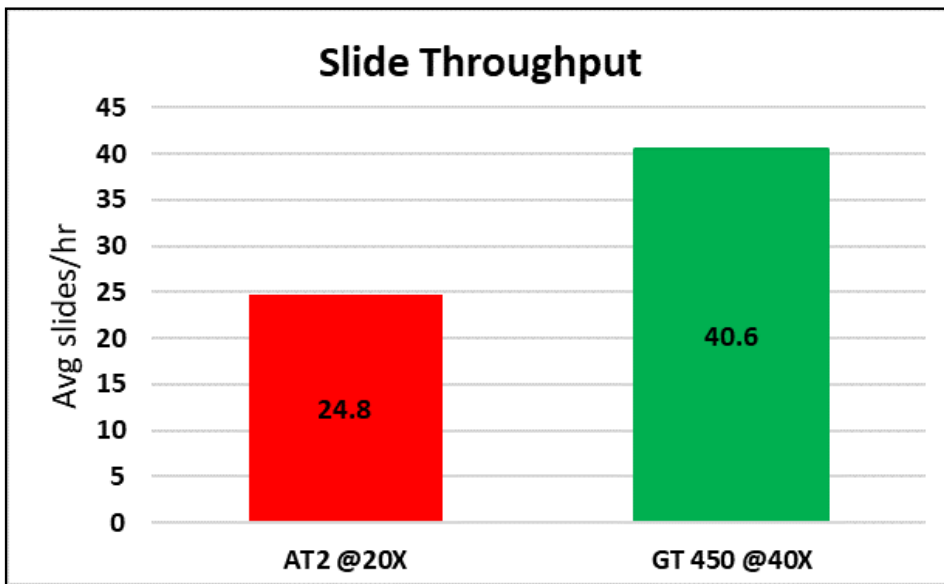
64% Improvement.

Total throughput is defined as the number of slides per hour that each instrument could process all workflow

steps from start to finish. This included all ancillary steps such as image QC and hands-on time.

Table 3 (below): Throughput data for Aperio AT2 at 20x and Aperio GT 450 at 40x. The Aperio GT 450 is 64% faster in TAT.

<b>AT2 @ 20x</b>	<b>Run 1</b>	<b>Run 2</b>	<b>Run 3</b>	<b>Avg</b>
Total throughput (slides/hr)	25.6	22.7	26.1	24.8
<b>GT 450 @ 40x</b>	<b>Run 4</b>	<b>Run 5</b>	<b>Run 6</b>	<b>Avg</b>
Total throughput (slides/hr)	39.3	40.3	42.2	40.6



**Figure 4 (above):** Throughput comparisons. The Aperio GT 450 shows an average throughput of 41 slides per hour at 40X magnification, whereas the Aperio AT2 resulted in an average throughput of 25 slides per hour at 20X. Note that the scan magnifications differ yet significant improvements with Aperio GT 450 at 40x are still observed.

**Turnaround time (TAT)**

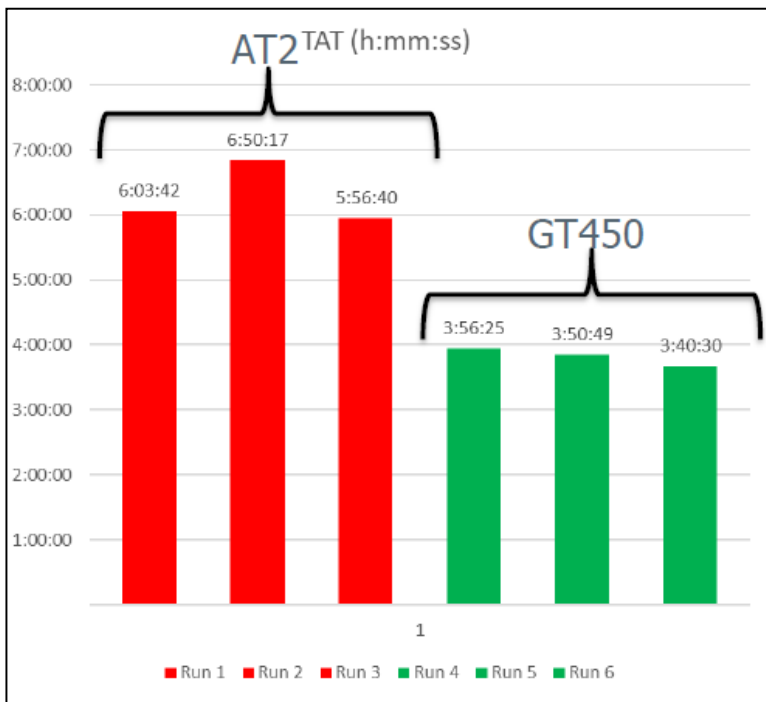
39% reduction.

The TAT for the run of 155 slides, which is defined as the total amount of time from start to finish of the workflow steps, indicates the Aperio GT 450 workflow steps taking

an average of 3 hours, 49 minutes, 15 seconds scanning at 40X. The Aperio AT2 workflow process TAT averaged 6 hours, 16 minutes, 53 seconds, scanning at 20X.

Table 4 (below): Total run time (expressed as TAT) for completing all workflow steps. Aperio GT 450 runs resulted in a 39% reduction versus Aperio AT2.

<b>AT2</b>	<b>Run 1</b>	<b>Run 2</b>	<b>Run 3</b>	<b>Avg</b>
Turnaround Time (TAT) in h:mm:ss	6:03:42	6:50:17	5:56:40	6:16:53
<b>GT 450</b>	<b>Run 4</b>	<b>Run 5</b>	<b>Run 6</b>	<b>Avg</b>
Turnaround Time (TAT) in h:mm:ss	3:56:25	3:50:49	3:40:30	3:49:15



**Figure 5 (above):** Turnaround time (TAT) to complete all workflow steps by run for Aperio AT2 and Aperio GT 450.

**Image quality**

Excellent image quality.

Both Aperio AT2 and Aperio GT 450 resulted in excellent image quality scores. Data was reported as average image quality score for each run of 155 slides reviewed by Pathologists by scanner model. No image quality scores

for any run on Aperio AT2 or Aperio GT 450 received a score of less than 3 and all images for both Aperio AT2 and Aperio GT 450 were considered to be of excellent image quality and suitable for the workflow needs.

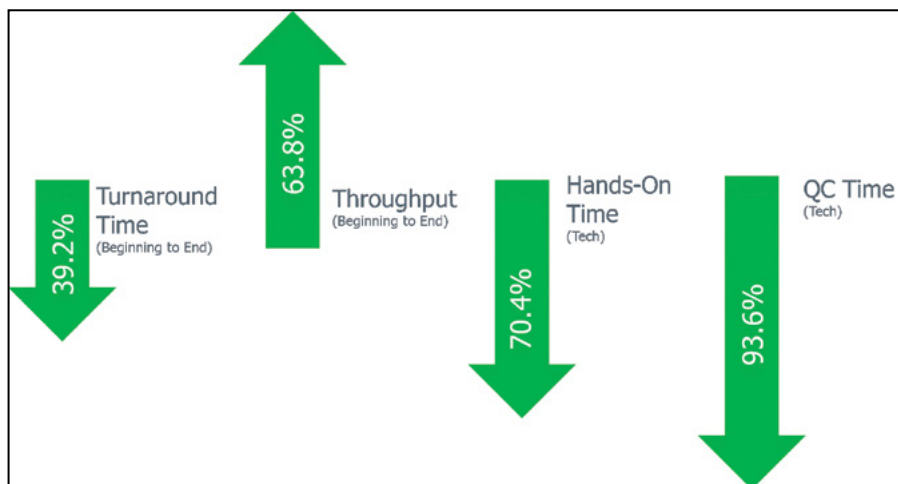
Table 5 (below): Average image quality scores by Pathologist by scanner model. Both scanner models resulted in excellent image quality.

Scanner Model	Pathologist #1 Run #1	Pathologist #2 Run #2	Pathologist #3 Run #3	Average IQ score across all AT2 runs
Aperio AT2 IQ score	4.0	4.0	4.0	4.0
	Pathologist #1 Run #4	Pathologist #2 Run #5	Pathologist #3 Run #6	Average IQ score across all GT 450 runs
Aperio GT 450 IQ Score	4.0	4.0	3.9	4.0

**Conclusion**

The Aperio GT 450 provides quantifiable and substantial workflow improvements while maintaining excellent image quality for which NeoGenomics can benefit to scale up their digital pathology operations.

Specifically, introducing the Aperio GT 450 into the workflow resulted in 94% reduction in QC tech time, 70% reduction in hands-on time, while improving throughput by 64% and reducing TAT by 39%.



**Figure 6 (above):** Summarized study endpoints.

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