

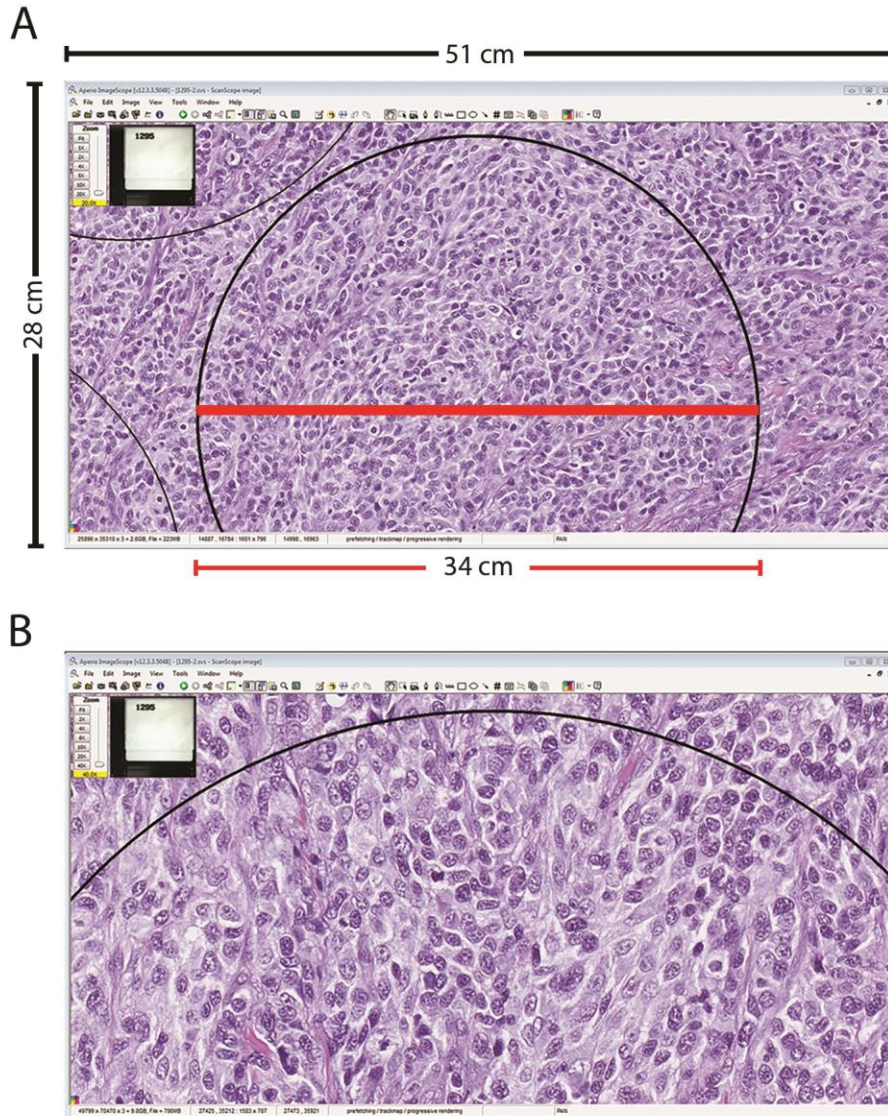
Supplemental Table 1. Study design and accomplished case examinations by study pathologists.

Modality		CM40x			WSI20x			WSI40x		
Case Groups		1	2	3	1	2	3	1	2	3
	n	38	38	37	38	38	37	38	38	37
Observer										
•		X	X			X	X		X	
•			X	X	X		X			X
•		X		X	X	X		X		
•		X		X	X	X		X		
•		X		X	X	X		X		
•			X	X	X		X			X
•		X		X	X	X		X		
•			X	X	X		X			X
•		X	X			X	X		X	
•		X	X			X	X		X	
•			X	X	X		X			X

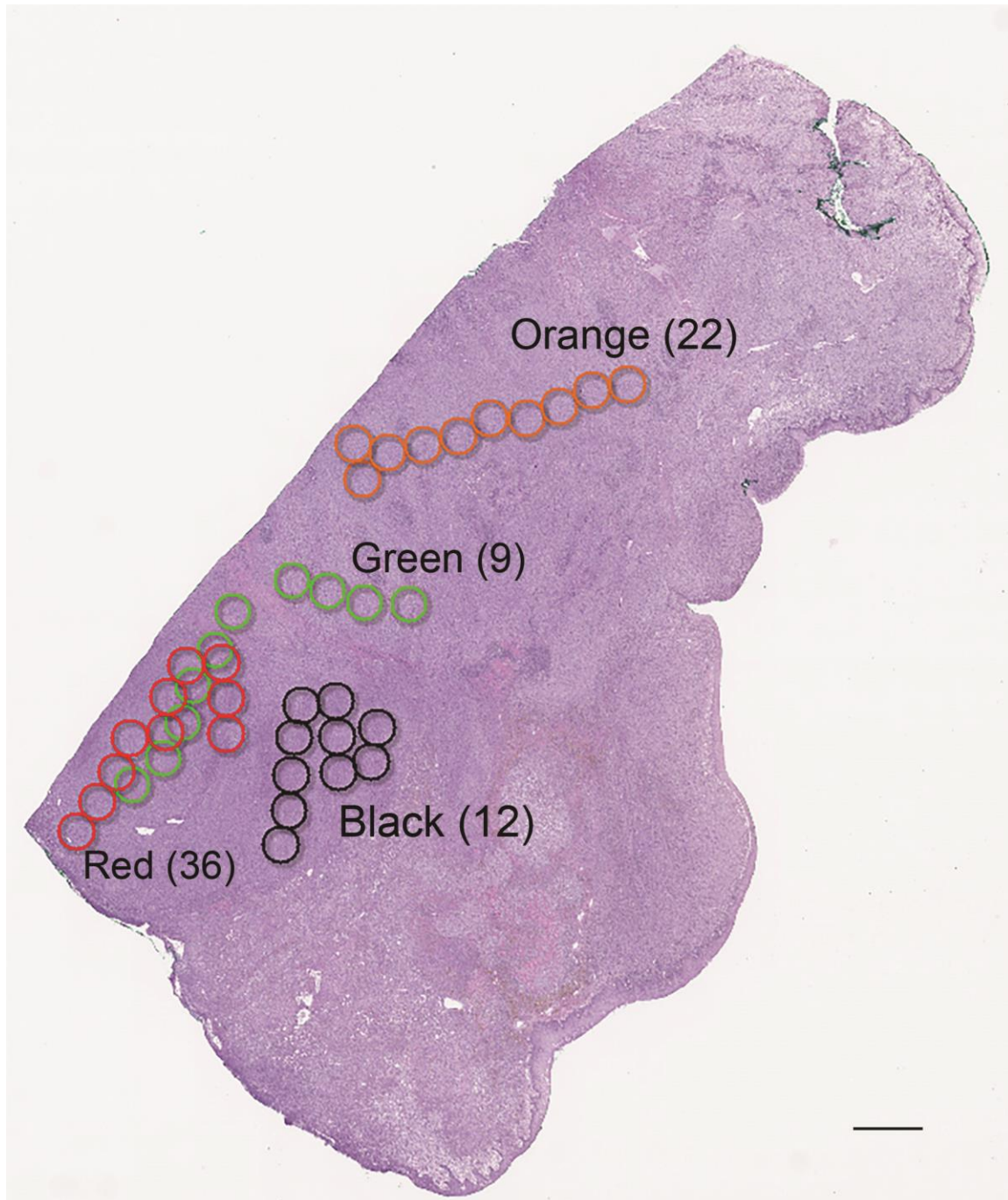
Case groups 1 - 3 represent all patients divided randomly and approximately evenly into 3 groups (n = 37 or 38 per case group). X, case assignments for each pathologist, for each microscopy modality. Gray shaded area indicates censored data, due to an observer deviation from the study protocol. (• = Individual observer)

Supplemental Table 2. Study display monitor and microscope specifications

Computer Display Model	Display Size (diagonal)	Display Resolution	Display Pixel Size (mm)	Display Pixel Density (pixels/inch)	Microscope Field Number	Field of View (FOV)
View Sonic Model # VS14768	22 inches	1920 x 1080	0.269	94.339	22 mm	0.237 mm ²
Dell Professional Model # P2213	22 inches	1680 x 1050	0.282	90.051	22 mm	0.237 mm ²
Dell Professional Model # P2210	22 inches	1680 x 1050	0.282	90.051	22 mm	0.237 mm ²
HP Compaq Model # LA2306x	23 inches	1920 x 1080	0.265	95.778	22 mm	0.237 mm ²
ViewSonic Model # VG2230wm	22 inches	1680 x 1050	0.282	90.051	22 mm	0.237 mm ²
Dell Professional Model # P2314H	23 inches	1920 x 1080	0.265	95.778	22 mm	0.237 mm ²
Dell Professional Model # P2210	22 inches	1680 x 1050	0.282	90.051	20 mm	0.196 mm ²
Dell UltraSharp Model # 1907FP	19 inches	1280 x 1024	0.294	86.273	22 mm	0.237 mm ²
Samsung SyncMaster Model # 2443BWT	24 inches	1920 x 1200	0.269	94.339	22 mm	0.237 mm ²
Apple iMac (Spring 2011)	21.5 inches	1920 x 1080	0.247	102.460	22 mm	0.237 mm ²

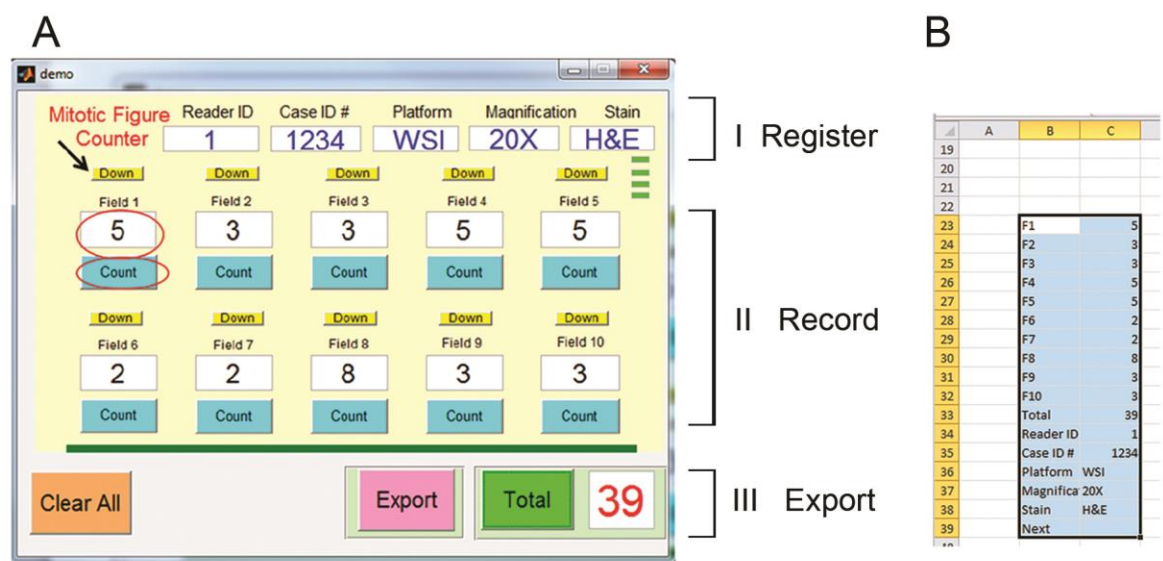


Supplemental Figure S1. Relative fields of view used to quantify mitotic figures in tumors in digital mode, as appeared on 22-inch diagonal computer display (dimensions indicated) of (A) WSI20x and (B) WSI40x, at maximum projected resolution. Inset circles (black lines) represent annotated area equivalent to a high-power (40x objective) field of view under conventional microscope; in this example representation is relative to a 22mm diameter ocular lens field number (working diameter 550 μ m).

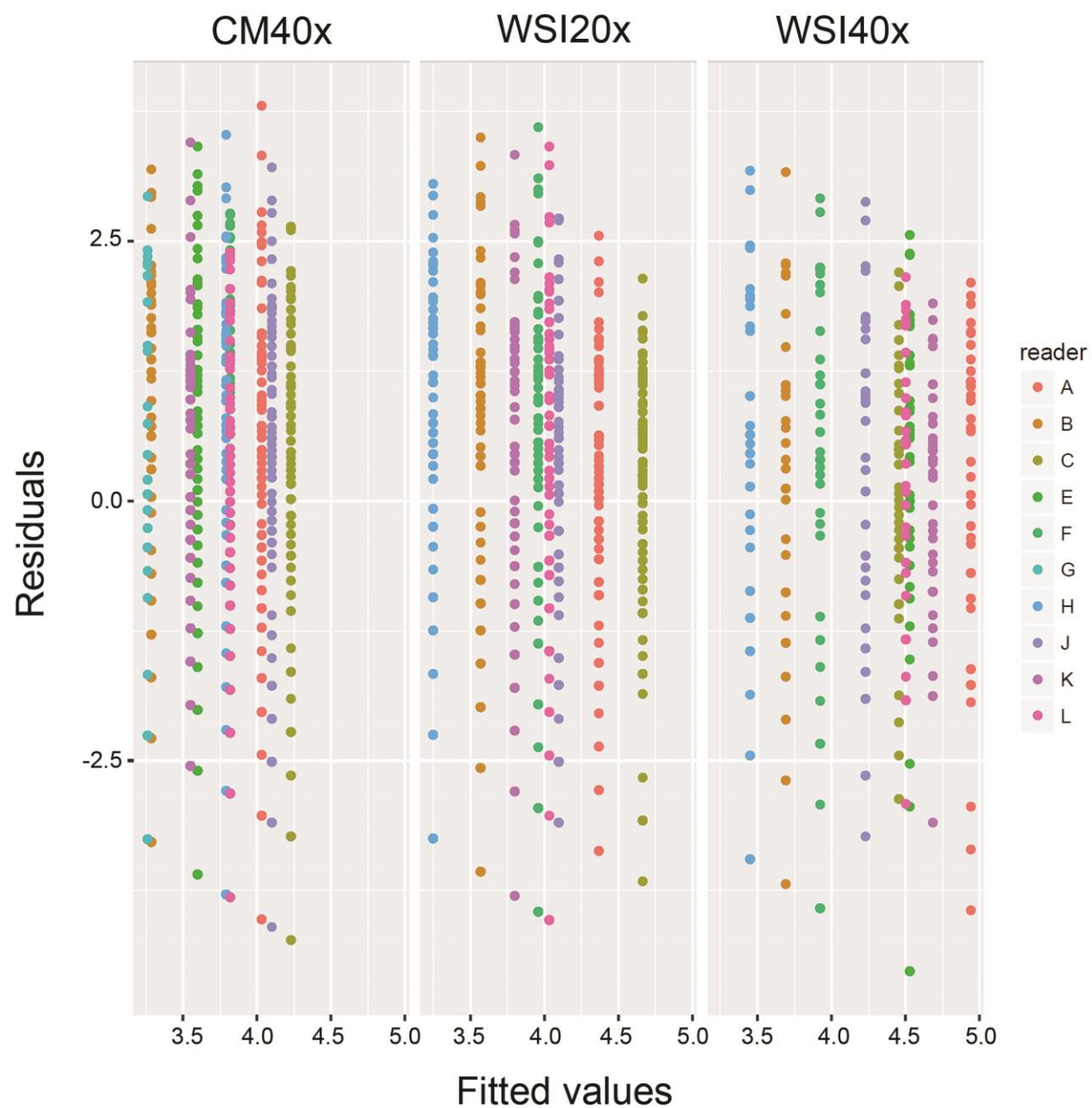


Supplemental Figure S2. Example image overlay depicting locations of hot spot-annotated ROI for determining mitotic activity counts from four pathologists, for one H&E-stained melanoma case. The ten fields of view (FOV) corresponding to the

pathologists' 40x objective lens field number, chosen independently by each pathologist for counting MF, are color coded and shown accompanied by total MF counts recorded. In this example overlay that was selected to depict disparities among multiple pathologist assessments, which occurred for some cases, one pathologist observer MF count (green) reflected less than the established cut point of ten MF, as compared to the other three pathologists with varying counts exceeding the cut point (range 12 to 36 MF in ten FOV). Bar = 1mm. Hematoxylin and eosin.

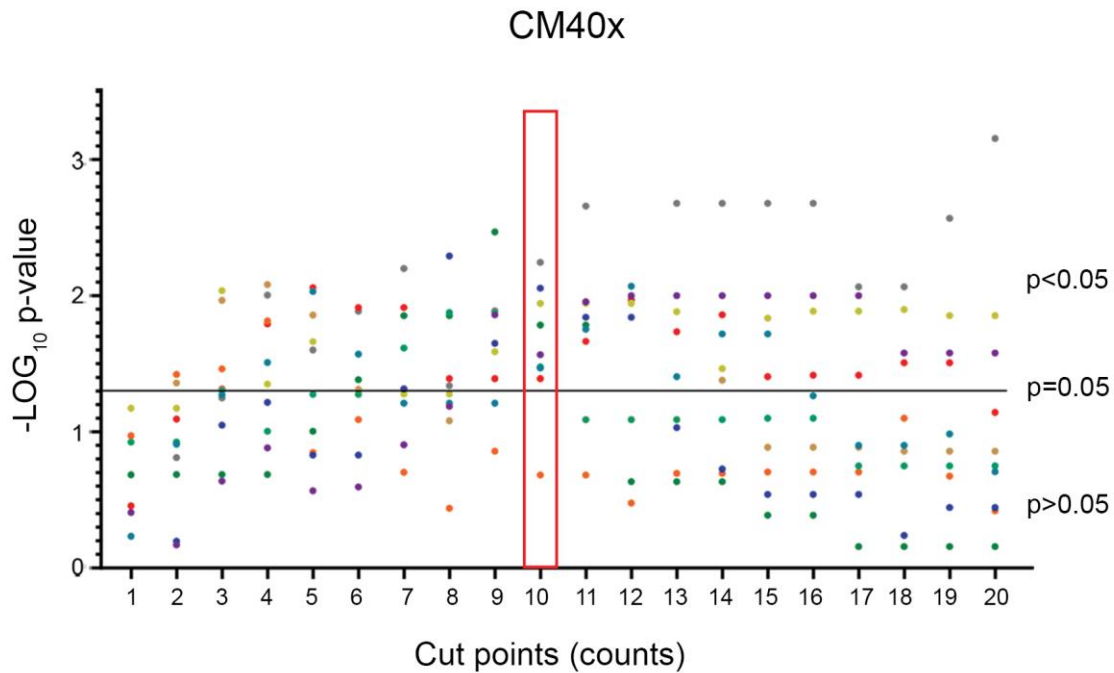


Supplemental Figure S3. Front panel of (A) Graphical User Interface (GUI), and (B) spreadsheet designed for recording counts. Three-phase function (I, II, III) is described in materials and methods. Recordation of MF counts was executed with the count key (circles), which could be adjusted down if necessary (arrow).



Supplemental Figure S4. ANOVA residual analysis of pathologist observer derived mitotic figure count values. Residuals versus fits plots (data transformed by the function

$\log_{10}(\text{MF counts}+1)$) depict an even distribution of fitted values. The distribution of residuals (differences between each case MF count and the fitted value, y axis) are similar for pathologists across all modalities. In these, both observer and modality had significant effect on the MF counts, however the interaction of the two factors had no significant effect on the MF counts.



Supplemental Figure S5. Optimal mitotic count cut point determination. Continuous mitotic figure (MF) values from CM ($X = 1 - 20$) were serially applied to divide cases into two groups, cases with $\text{MF} \geq X$ vs. those cases with $\text{MF} < X$. p-values from Kaplan-

Meier survival curve analyses were generated for mitotic counts from each pathologist. This is plotted against the presumptive cut points (from ten FOV) on the x axis, (color dots are unique pathologist observers, n = from 7 to 10). Based upon this plot, a count of ≥ 10 mitotic figures was selected (red rectangle) for predicting difference in survival outcome, founded upon greatest probability of overall pathologist agreement; i.e., at cut point = 10, nine of ten pathologists successfully separated the case groups that exhibited significant difference in low vs. high survival risk, ($p < 0.05$).