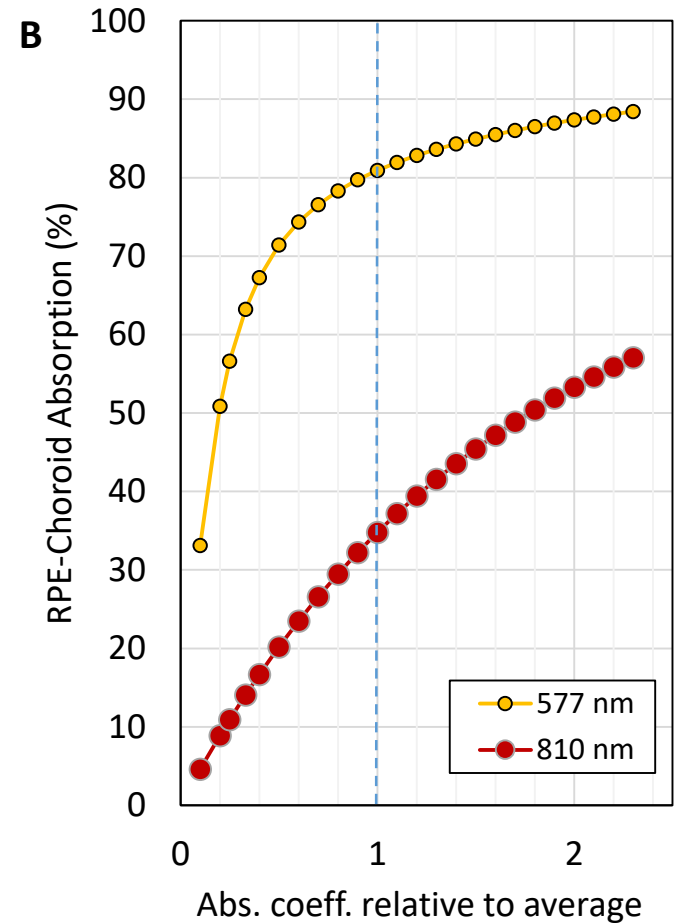
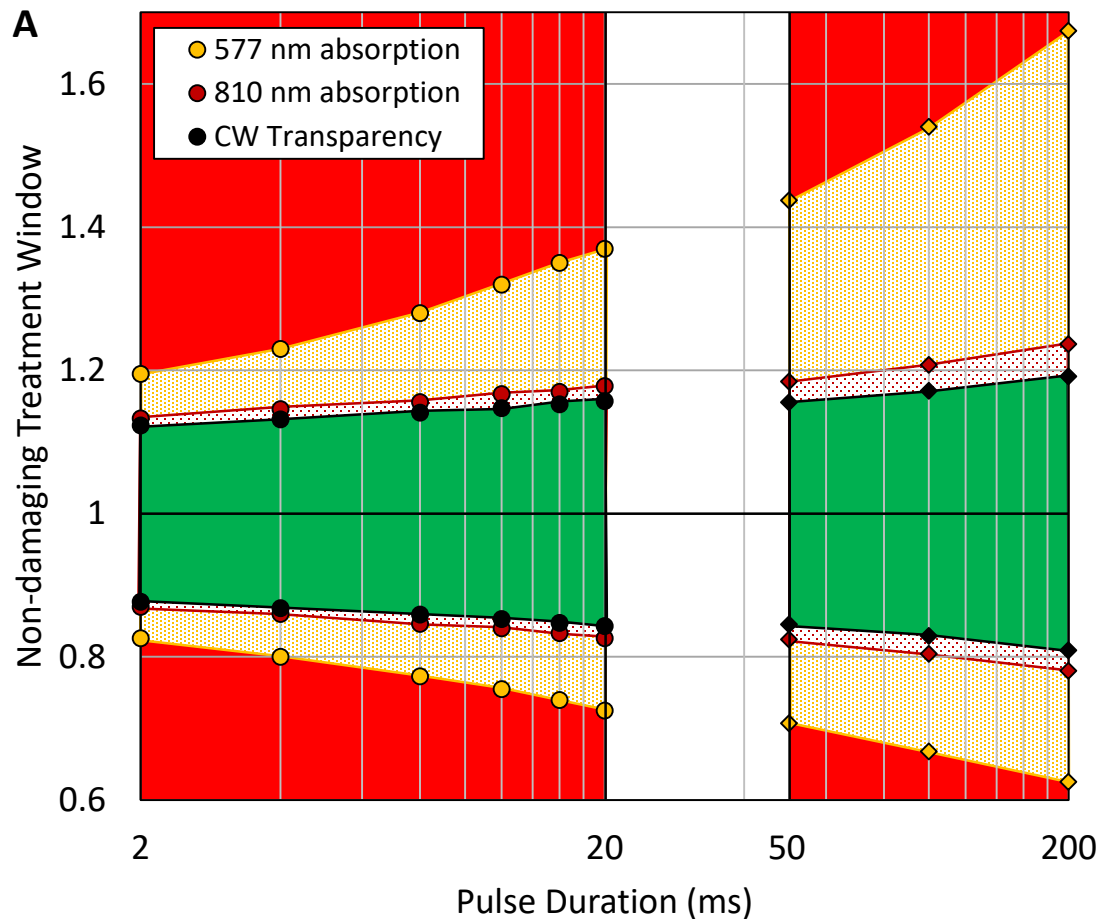
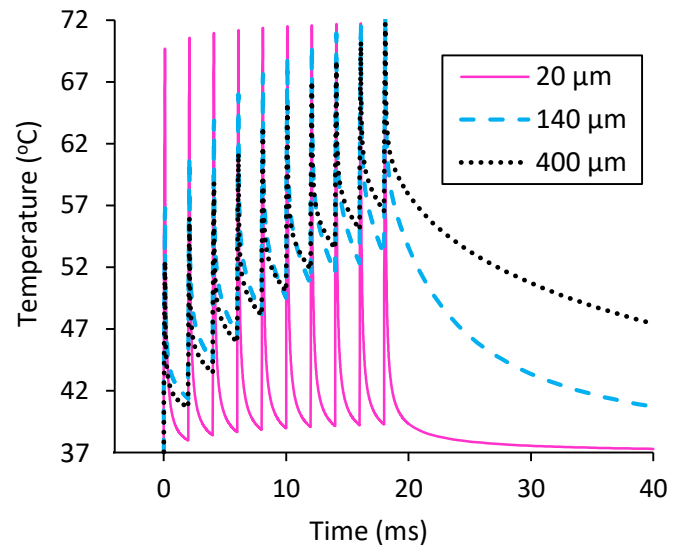


Micropulse Duty Cycle	Total spots (200 ms)	# of eyes (200 ms)	Total spots (20 ms)	# of eyes (20 ms)
100%	269	10	440	13
47%	109	4	110	4
25%	131	5	114	4
15%	120	4	130	5
12%	51	2	NA	NA
9%	50	2	110	4
6%	NA	NA	57	2
5%	140	5	160	3
3%	139	5	135	5

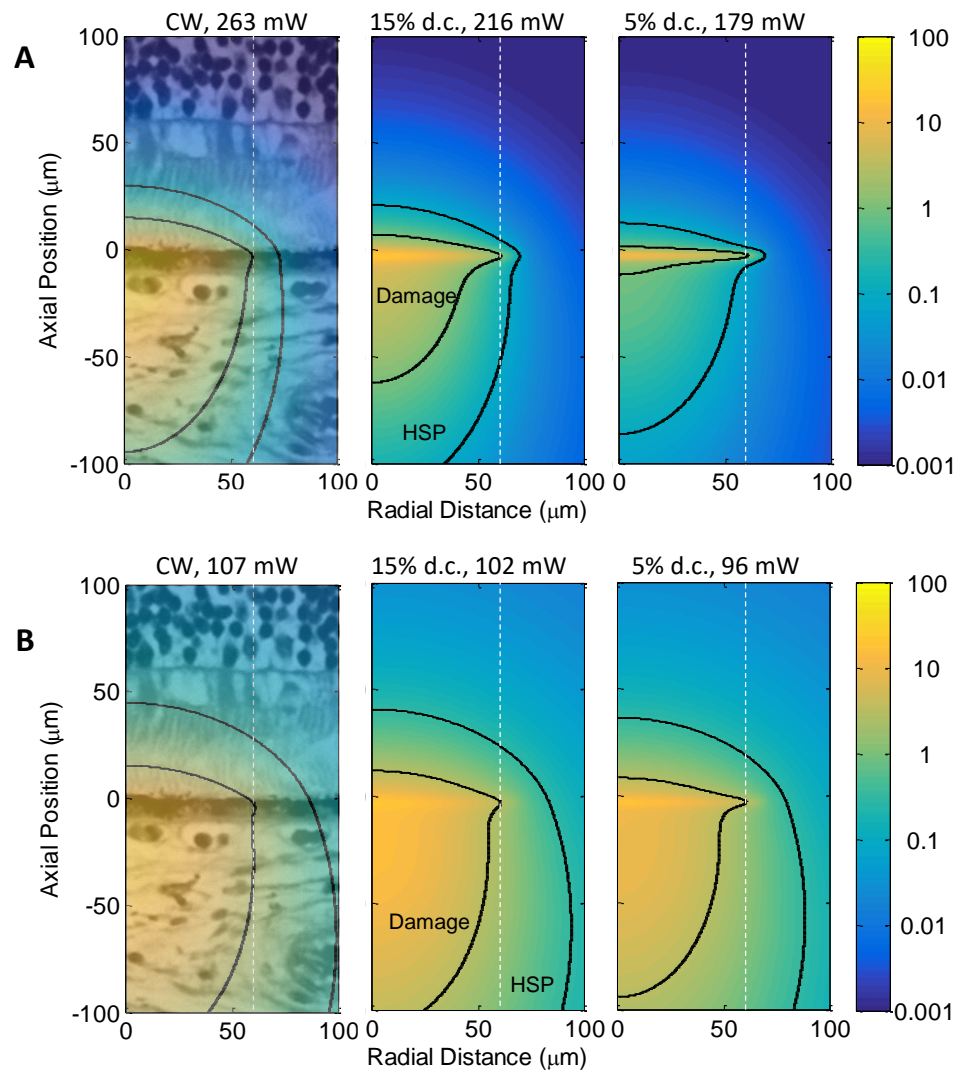
Supplemental Table 1. Number of experimental lesions delivered in rabbit experiments. Total # of spots spanned three thresholds: immediate ophthalmoscopic visibility (IV), delayed visibility (DV), and fluorescein angiography visibility (FA). Approximately 1/3 of spots delivered at a given duty cycle and pulse duration were significant in the determination of each type of damage threshold.



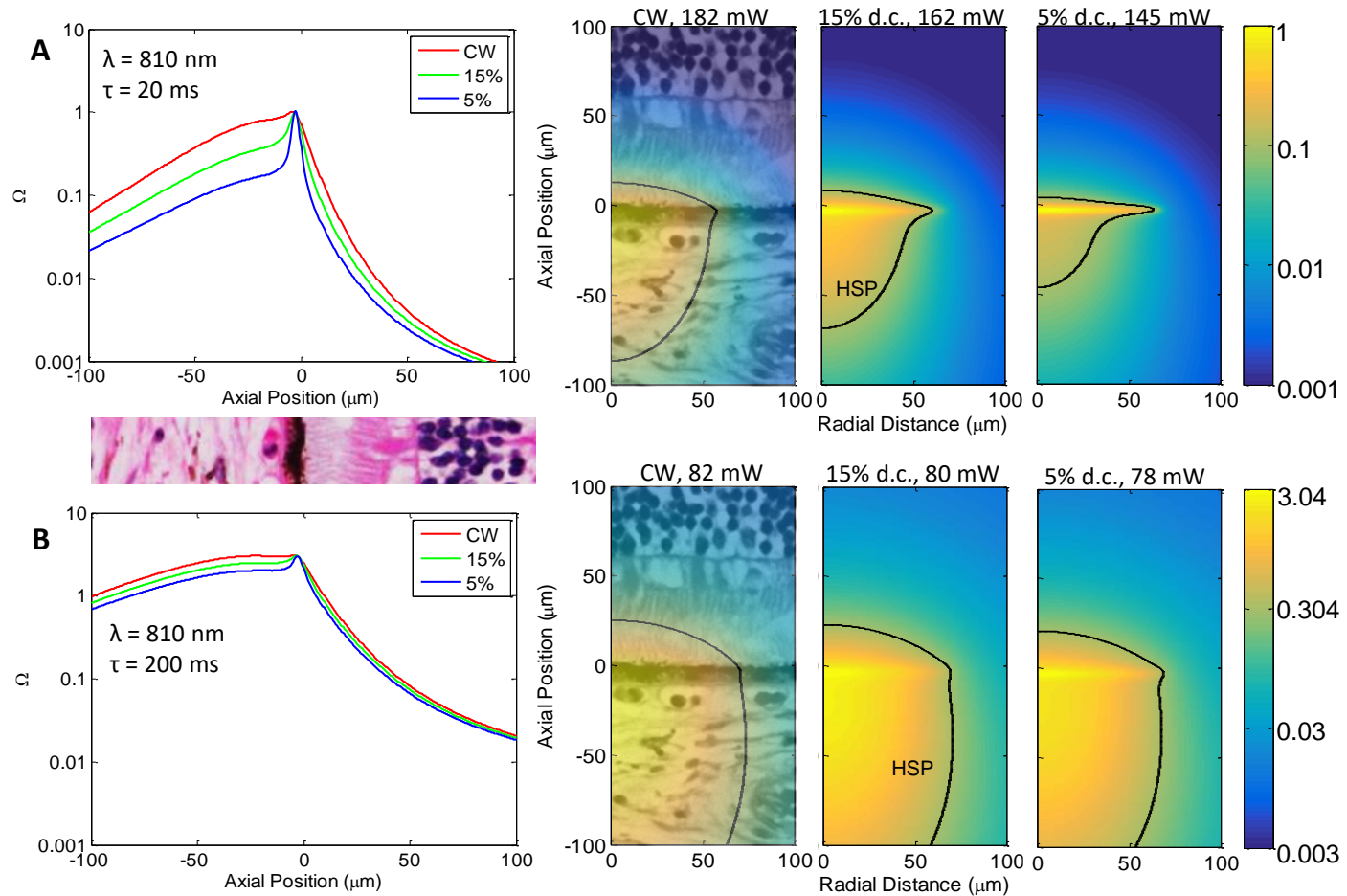
Supplemental Figure 1. (A) Tolerance to variation in pigmentation and transparency for CW non-damaging retinal laser therapy. Yellow and red markers indicate maximum variation in pigmentation, as defined by variation in RPE and choroidal absorption coefficient, before the treatment becomes damaging or sub-therapeutic for 577 nm and 810 nm wavelengths, respectively. Black markers indicate maximum variation in ocular transparency. Treatment with 5% duty cycle micropulse modulation would show reduced tolerance to pigmentation variation deriving from the reduced tolerance to absorbed power shown in Figure 8. Treatment range was calculated assuming Arrhenius parameters, $\Omega_{\text{damage}} = 1$ and $\Omega_{\text{HSP}} = 0.1$ for pulse durations of 2 - 20 ms (shown with circles), and $\Omega_{\text{damage}} = 3.04$ and $\Omega_{\text{HSP}} = 0.304$ for 50 - 200 ms (shown with diamonds). (B) Total absorption in RPE-Choroid layer as a function of deviation of absorption coefficient from average for 810 nm and 577 nm wavelengths. Changes in tissue pigmentation, as modeled by absorption coefficient, act nearly linearly on the total absorption only when the absorption coefficient is low, which holds true for 810nm, but not for much shorter wavelengths.



Supplemental Figure 2. RPE temperature in the center of laser beam calculated for 577 nm laser at 5% duty cycle and 20 ms pulse duration with the damage threshold powers: 1.7 mW for 20 μm beam (solid magenta), 24.6 mW for 140 μm (dashed yellow), and 150.8 mW for 400 μm (dotted black).



Supplemental Figure 3. Spatial distribution of the Arrhenius integral across the retina and choroid in human model after FA threshold laser treatment with 810 nm laser in 140 μm spot at the labeled duty cycle and average power for (A) 20 ms and (B) 200 ms pulse envelope. Black line contours show onset of HSP expression (outside) and cellular damage (inside). White dotted lines at 60 μm radius show correlation radius for translating model to FA threshold in experiment. Left-most panel shows overlay of human photoreceptors, RPE, and choroid.



Supplemental Figure 4. Spatial distribution of the Arrhenius integral across the retina and choroid in human model just below damage threshold with 810 nm laser in 140 μm spot at the labeled duty cycle and average power for (A) 20 ms and (B) 200 ms pulse envelope. Black contour shows the area above the HSP expression threshold. Plot on the left shows axial variation of Ω at center of the laser beam, with 0 axial position corresponding to the top of the RPE layer, as illustrated with histology of the human photoreceptors, RPE, and choroid set along the x-axis.