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Table SI. Vascular differences between treatment-resistant and treatment responsive AK I-II					
Baseline	AK I-II	Resistant			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	21	144.02	104.31	186.62
	Vessel area density (%)	21	27.71	18.40	34.20
	Mean vessel length (µm)	21	151.00	138.50	167.50
	Mean vessel diameter (µm)	21	45.82	43.56	48.30
	Branchpoint density (nodes/mm*2)	21	3.15	2.25	3.80
	Mean tortuosity	21	1.14	1.14	1.16
	Fractal dimension	21	1.40	1.34	1.45
Month 3		Resistant			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	20	126.11	78.91	148.45
	Vessel area density (%)	20	23.91	16.39	27.82
	Mean vessel length (µm)	20	161.00	149.00	182.00
	Mean vessel diameter (µm)	20	47.57	43.61	48.01
	Branchpoint density (nodes/mm*2)	20	2.43	2.02	3.31
	Mean tortuosity (NA)	20	1.15	1.14	1.16
	Fractal dimension (NA)	20	1.38	1.30	1.41
Month 12		Resistant			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	21	102.58	80.45	158.11
	Vessel area density (%)	21	21.19	16.11	29.62
	Mean vessel length (µm)	21	165.00	154.50	179.00
	Mean vessel diameter (µm)	21	46.05	43.29	48.53
	Branchpoint density (nodes/mm*2)	21	2.50	1.91	3.07
	Mean tortuosity (NA)	21	1.15	1.13	1.16

	Fractal dimension (NA)	21	1.34	1.31	1.42
Baseline	AK I-II	Cleared			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	34	120.90	86.94	143.03
	Vessel area density (%)	34	22.86	17.32	26.76
	Mean vessel length (µm)	34	160.00	152.00	169.25
	Mean vessel diameter (µm)	34	45.01	42.06	48.12
	Branchpoint density (nodes/mm*2)	34	2.63	2.17	3.04
	Mean tortuosity	34	1.16	1.14	1.17
	Fractal dimension	34	1.37	1.31	1.40
Month 3		Cleared			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	33	101.36	75.89	141.35
	Vessel area density (%)	33	20.18	15.91	26.15
	Mean vessel length (µm)	33	170.00	148.75	182.25
	Mean vessel diameter (µm)	33	46.20	43.11	48.04
	Branchpoint density (nodes/mm*2)	33	2.26	1.75	3.15
	Mean tortuosity (NA)	33	1.15	1.14	1.17
	Fractal dimension (NA)	33	1.34	1.30	1.40
Month 12		Cleared			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	34	141.84	99.69	164.78
	Vessel area density (%)	34	26.00	19.34	32.69
	Mean vessel length (µm)	34	166.50	146.00	172.00
	Mean vessel diameter (µm)	34	47.22	44.47	50.12
	Branchpoint density (nodes/mm*2)	34	2.59	2.09	3.43
	Mean tortuosity (NA)	34	1.14	1.13	1.16
	Fractal dimension (NA)	34	1.40	1.34	1.43
Baseline	PD	PD			
		N	Median	Percentiles	

		Valid		25	75
	Total vessel length (µm)	35	111.34	76.28	133.86
	Vessel area density (%)	35	21.47	16.02	26.34
	Mean vessel length (µm)	35	170.00	156.00	185.00
	Mean vessel diameter (µm)	35	44.65	42.69	49.08
	Branchpoint density (nodes/mm*2)	35	2.25	1.75	2.99
	Mean tortuosity	35	1.14	1.13	1.16
	Fractal dimension	35	1.36	1.30	1.39
Month 3		PD			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	34	109.94	87.02	126.68
	Vessel area density (%)	34	21.94	18.40	25.39
	Mean vessel length (µm)	34	172.00	156.00	177.00
	Mean vessel diameter (µm)	34	47.24	44.75	48.93
	Branchpoint density (nodes/mm*2)	34	2.38	1.88	3.08
	Mean tortuosity (NA)	34	1.14	1.13	1.16
	Fractal dimension (NA)	34	1.36	1.32	1.38
Month 12		PD			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	35	132.06	103.87	155.52
	Vessel area density (%)	35	25.37	20.70	28.91
	Mean vessel length (µm)	35	161.00	149.00	172.00
	Mean vessel diameter (µm)	35	47.62	45.67	49.75
	Branchpoint density (nodes/mm*2)	35	2.75	2.10	3.47
	Mean tortuosity (NA)	35	1.14	1.13	1.15
	Fractal dimension (NA)	35	1.39	1.35	1.42

This table provides descriptive data for vascular parameters in treatment-resistant and treatment-responsive actinic keratosis (AK) grades I-II, and photodamaged skin (PD). Values are presented as median with interquartile range (IQR).

Table SII. Vascular differences between treatment-resistant and treatment responsive AK, split by AK grade

Baseline	Treatment response	Resistant			
	Lesion group	AK I			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	13	107.07	73.96	186.62
	Vessel area density (%)	13	19.50	15.65	35.03
	Mean vessel length (µm)	13	158.00	142.00	173.00
	Mean vessel diameter (µm)	13	43.77	39.43	49.18
	Branchpoint density (nodes/mm*2)	13	2.31	1.56	3.80
	Mean tortuosity	13	1.14	1.14	1.17
	Fractal dimension	13	1.35	1.29	1.45
Month 3	Treatment response	Resistant			
	Lesion group	AK I			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	12	126.11	43.94	154.22
	Vessel area density (%)	12	23.91	9.23	27.97
	Mean vessel length (µm)	12	163.00	149.50	188.50
	Mean vessel diameter (µm)	12	46.79	41.07	48.01
	Branchpoint density (nodes/mm*2)	12	2.43	1.53	3.25
	Mean tortuosity	12	1.15	1.14	1.17
	Fractal dimension	12	1.38	1.21	1.41
Month 12	Treatment response	Resistant			
	Lesion group	AK I			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	13	86.42	76.67	130.95
	Vessel area density (%)	13	18.78	15.46	24.88
	Mean vessel length (µm)	13	169.00	161.00	181.50
	Mean vessel diameter (µm)	13	45.94	41.70	48.32
	Branchpoint density (nodes/mm*2)	13	2.11	1.62	2.73

	Mean tortuosity	13	1.16	1.13	1.17
	Fractal dimension	13	1.32	1.30	1.38
Baseline	Treatment response	Cleared			
	Lesion group	AK I			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	24	113.91	81.46	134.97
	Vessel area density (%)	24	22.82	17.25	25.89
	Mean vessel length (µm)	24	162.00	152.50	169.00
	Mean vessel diameter (µm)	24	45.01	42.21	47.94
	Branchpoint density (nodes/mm*2)	24	2.61	2.11	2.98
	Mean tortuosity	24	1.16	1.14	1.17
	Fractal dimension	24	1.37	1.31	1.39
Month 3	Treatment response	Cleared			
	Lesion group	AK I			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	23	102.32	74.92	142.50
	Vessel area density (%)	23	20.18	15.31	28.27
	Mean vessel length (µm)	23	170.50	149.25	181.50
	Mean vessel diameter (µm)	23	46.45	43.64	48.39
	Branchpoint density (nodes/mm*2)	23	2.26	1.70	3.38
	Mean tortuosity	23	1.14	1.13	1.17
	Fractal dimension	23	1.34	1.29	1.40
Month 12	Treatment response	Cleared			
	Lesion group	AK I			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	24	143.68	100.34	171.43
	Vessel area density (%)	24	27.54	19.15	32.90
	Mean vessel length (µm)	24	159.00	146.25	171.00
	Mean vessel diameter (µm)	24	47.22	44.66	50.34
	Branchpoint density (nodes/mm*2)	24	2.75	2.12	3.41

	Mean tortuosity	24	1.14	1.13	1.16
	Fractal dimension	24	1.40	1.34	1.43
Baseline	Treatment response	Resistant			
	Lesion group	AK II			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	8	159.36	134.33	190.99
	Vessel area density (%)	8	29.92	25.28	33.58
	Mean vessel length (µm)	8	141.00	134.00	154.75
	Mean vessel diameter (µm)	8	46.80	45.96	47.97
	Branchpoint density (nodes/mm*2)	8	3.65	2.94	3.98
	Mean tortuosity	8	1.14	1.14	1.15
	Fractal dimension	8	1.42	1.39	1.45
Month 3	Treatment response				
	Lesion group	AK II			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	8	118.75	90.29	143.60
	Vessel area density (%)	8	24.44	17.50	27.47
	Mean vessel length (µm)	8	159.00	149.00	183.25
	Mean vessel diameter (µm)	8	47.57	44.92	48.14
	Branchpoint density (nodes/mm*2)	8	2.68	2.12	3.39
	Mean tortuosity	8	1.14	1.13	1.15
	Fractal dimension	8	1.37	1.33	1.40
Month 12	Treatment response				
	Lesion group	AK II			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	8	145.97	104.50	164.83
	Vessel area density (%)	8	27.27	20.27	30.73
	Mean vessel length (µm)	8	157.50	142.50	173.25
	Mean vessel diameter (µm)	8	46.35	44.32	48.72
	Branchpoint density (nodes/mm*2)	8	2.89	2.39	3.24

	Mean tortuosity	8	1.14	1.14	1.15
	Fractal dimension	8	1.40	1.35	1.42
Baseline	Treatment response	Cleared			
	Lesion group	AK II			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	10	127.37	86.14	159.98
	Vessel area density (%)	10	23.24	18.03	30.17
	Mean vessel length (µm)	10	155.00	150.00	180.00
	Mean vessel diameter (µm)	10	44.82	41.57	49.64
	Branchpoint density (nodes/mm*2)	10	2.83	2.14	3.19
	Mean tortuosity	10	1.16	1.14	1.17
	Fractal dimension	10	1.38	1.32	1.42
Month 3	Treatment response				
	Lesion group	AK II			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	10	96.35	75.90	121.90
	Vessel area density (%)	10	18.86	16.42	23.16
	Mean vessel length (µm)	10	169.00	148.75	185.50
	Mean vessel diameter (µm)	10	44.90	42.23	47.38
	Branchpoint density (nodes/mm*2)	10	2.30	1.75	2.91
	Mean tortuosity	10	1.15	1.14	1.17
	Fractal dimension	10	1.34	1.30	1.38
Month 12	Treatment response				
	Lesion group	AK II			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	10	138.11	94.68	154.37
	Vessel area density (%)	10	24.90	19.59	29.38
	Mean vessel length (µm)	10	169.00	141.00	177.50
	Mean vessel diameter (µm)	10	47.46	42.12	50.38
	Branchpoint density (nodes/mm*2)	10	2.59	2.01	3.70

	Mean tortuosity	10	1.14	1.12	1.16
	Fractal dimension	10	1.40	1.33	1.41
Baseline	Treatment response	Resistant			
	Lesion group	AK III			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	5	54.22	27.55	123.32
	Vessel area density (%)	5	11.85	5.37	23.64
	Mean vessel length (µm)	5	161.00	140.00	178.50
	Mean vessel diameter (µm)	5	43.28	39.18	49.12
	Branchpoint density (nodes/mm*2)	5	2.18	1.33	3.35
	Mean tortuosity	5	1.15	1.13	1.16
	Fractal dimension	5	1.25	1.11	1.38
Month 3	Treatment response	Resistant			
	Lesion group	AK III			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	5	92.44	82.56	125.21
	Vessel area density (%)	5	17.53	17.17	25.10
	Mean vessel length (µm)	5	160.00	139.00	177.00
	Mean vessel diameter (µm)	5	46.37	44.57	50.09
	Branchpoint density (nodes/mm*2)	5	2.65	2.08	3.24
	Mean tortuosity	5	1.15	1.14	1.15
	Fractal dimension	5	1.32	1.32	1.37
Month 12	Treatment response	Resistant			
	Lesion group	AK III			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	5	63.77	44.50	107.69
	Vessel area density (%)	5	12.29	9.08	22.61
	Mean vessel length (µm)	5	162.00	151.50	175.00
	Mean vessel diameter (µm)	5	41.93	36.95	47.43
	Branchpoint density (nodes/mm*2)	5	2.09	1.39	2.68

	Mean tortuosity	5	1.16	1.14	1.18
	Fractal dimension	5	1.27	1.21	1.35
Baseline	Treatment response	Cleared			
	Lesion group	AK III			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	2	84.36	30.47	.
	Vessel area density (%)	2	15.38	6.46	.
	Mean vessel length (µm)	2	153.00	133.00	.
	Mean vessel diameter (µm)	2	40.88	34.87	.
	Branchpoint density (nodes/mm*2)	2	2.30	0.59	.
	Mean tortuosity	2	1.15	1.15	.
	Fractal dimension	2	1.27	1.15	.
Month 3	Treatment response	Cleared			
	Lesion group	AK III			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	2	64.00	37.92	.
	Vessel area density (%)	2	12.71	7.86	.
	Mean vessel length (µm)	2	181.50	177.00	.
	Mean vessel diameter (µm)	2	41.73	39.53	.
	Branchpoint density (nodes/mm*2)	2	1.52	1.13	.
	Mean tortuosity	2	1.14	1.13	.
	Fractal dimension	2	1.26	1.19	.
Month 12	Treatment response	Cleared			
	Lesion group	AK III			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	2	161.68	157.92	.
	Vessel area density (%)	2	28.69	27.90	.
	Mean vessel length (µm)	2	170.50	164.00	.
	Mean vessel diameter (µm)	2	44.33	43.81	.
	Branchpoint density (nodes/mm*2)	2	2.56	2.39	.

	Mean tortuosity	2	1.15	1.13	.
	Fractal dimension	2	1.42	1.42	.
Baseline	Treatment response	PD skin			
	Lesion group	PD			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	35	111.34	76.28	133.86
	Vessel area density (%)	35	21.47	16.02	26.34
	Mean vessel length (µm)	35	170.00	156.00	185.00
	Mean vessel diameter (µm)	35	44.65	42.69	49.08
	Branchpoint density (nodes/mm*2)	35	2.25	1.75	2.99
	Mean tortuosity	35	1.14	1.13	1.16
	Fractal dimension	35	1.36	1.30	1.39
Month 3	Treatment response	PD skin			
	Lesion group	PD			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	34	109.94	87.02	126.68
	Vessel area density (%)	34	21.94	18.40	25.39
	Mean vessel length (µm)	34	172.00	156.00	177.00
	Mean vessel diameter (µm)	34	47.24	44.75	48.93
	Branchpoint density (nodes/mm*2)	34	2.38	1.88	3.08
	Mean tortuosity	34	1.14	1.13	1.16
	Fractal dimension	34	1.36	1.32	1.38
Month 12	Treatment response	PD skin			
	Lesion group	PD			
		N	Median	Percentiles	
		Valid		25	75
	Total vessel length (µm)	35	132.06	103.87	155.52
	Vessel area density (%)	35	25.37	20.70	28.91
	Mean vessel length (µm)	35	161.00	149.00	172.00
	Mean vessel diameter (µm)	35	47.62	45.67	49.75
	Branchpoint density (nodes/mm*2)	35	2.75	2.10	3.47

	Mean tortuosity	35	1.14	1.13	1.15
	Fractal dimension	35	1.39	1.35	1.42

This table provides descriptive data for vascular parameters in treatment-resistant and treatment-responsive actinic keratosis (AK) grades I-III, and photodamaged skin (PD). The parameters include total vessel length, vessel area density, mean vessel length and diameter, branchpoint density, mean tortuosity and fractal dimension. Values are presented as median with interquartile range (IQR).

Table SIII. P-values of Mann-Whitney U test comprising treatment-resistant versus treatment-responsive AK		
AK I-II		
Visit	Vascular parameter	Exact Sig. (2-tailed)
Baseline	Total vessel length (μm)	0.324
	Vessel area density (%)	0.399
	Mean vessel length (μm)	0.139
	Mean vessel diameter (μm)	0.655
	Branchpoint density (nodes/mm ²)	0.312
	Mean tortuosity	0.223
	Fractal dimension	0.344
Month 3	Total vessel length (μm)	0.486
	Vessel area density (%)	0.565
	Mean vessel length (μm)	0.787
	Mean vessel diameter (μm)	0.767
	Branchpoint density (nodes/mm ²)	0.565
	Mean tortuosity	0.800
	Fractal dimension	0.522
Month 12	Total vessel length (μm)	0.035
	Vessel area density (%)	0.046
	Mean vessel length (μm)	0.873
	Mean vessel diameter (μm)	0.062
	Branchpoint density (nodes/mm ²)	0.129
	Mean tortuosity	0.065
	Fractal dimension	0.037

AK I		
Visit	Vascular parameter	Exact Sig. (2-tailed)
Baseline	Total vessel length (µm)	0.582
	Vessel area density (%)	0.695
	Mean vessel length (µm)	0.700
	Mean vessel diameter (µm)	0.838
	Branchpoint density (nodes/mm*2)	0.894
	Mean tortuosity	0.599
	Fractal dimension	0.695
	Month 3	Total vessel length (µm)
Vessel area density (%)		0.913
Mean vessel length (µm)		0.906
Mean vessel diameter (µm)		0.610
Branchpoint density (nodes/mm*2)		0.987
Mean tortuosity		0.499
Fractal dimension		0.944
Month 12		Total vessel length (µm)
	Vessel area density (%)	0.072
	Mean vessel length (µm)	0.365
	Mean vessel diameter (µm)	0.109
	Branchpoint density (nodes/mm*2)	0.124
	Mean tortuosity	0.152
	Fractal dimension	0.072
	AK II	
Visit	Vascular parameter	Exact Sig. (2-tailed)
Baseline	Total vessel length (µm)	0.055
	Vessel area density (%)	0.055
	Mean vessel length (µm)	0.088
	Mean vessel diameter (µm)	0.237
	Branchpoint density (nodes/mm*2)	0.043
	Mean tortuosity	0.408
	Fractal dimension	0.068
	Month 3	Total vessel length (µm)

	Vessel area density (%)	0.315
	Mean vessel length (μm)	0.696
	Mean vessel diameter (μm)	0.165
	Branchpoint density (nodes/ mm^2)	0.237
	Mean tortuosity	0.122
	Fractal dimension	0.274
Month 12	Total vessel length (μm)	0.696
	Vessel area density (%)	0.573
	Mean vessel length (μm)	0.445
	Mean vessel diameter (μm)	0.829
	Branchpoint density (nodes/ mm^2)	0.762
	Mean tortuosity	0.829
	Fractal dimension	0.633
AK III		
Visit	Vascular parameter	Exact Sig. (2-tailed)
Baseline	Total vessel length (μm)	1.000
	Vessel area density (%)	1.000
	Mean vessel length (μm)	0.857
	Mean vessel diameter (μm)	0.571
	Branchpoint density (nodes/ mm^2)	0.857
	Mean tortuosity	1.000
	Fractal dimension	1.000
Month 3	Total vessel length (μm)	0.381
	Vessel area density (%)	0.571
	Mean vessel length (μm)	0.238
	Mean vessel diameter (μm)	0.190
	Branchpoint density (nodes/ mm^2)	0.095
	Mean tortuosity	1.000
	Fractal dimension	0.571
Month 12	Total vessel length (μm)	0.095
	Vessel area density (%)	0.190
	Mean vessel length (μm)	0.571
	Mean vessel diameter (μm)	0.857

	Branchpoint density (nodes/mm*2)	0.381
	Mean tortuosity	0.571
	Fractal dimension	0.095

AK: Actinic keratosis

Significant and near-significant findings are highlighted in bold.