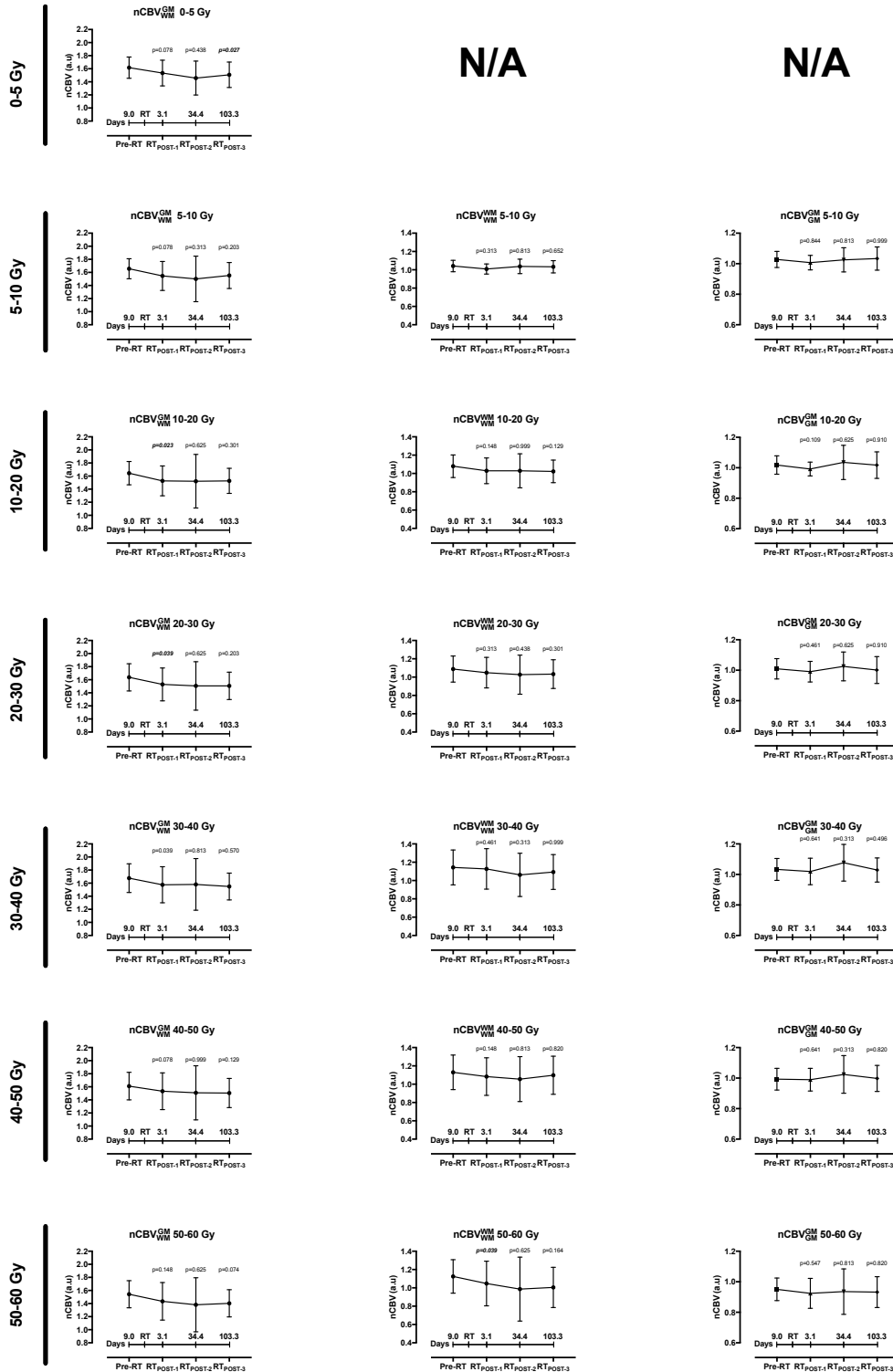


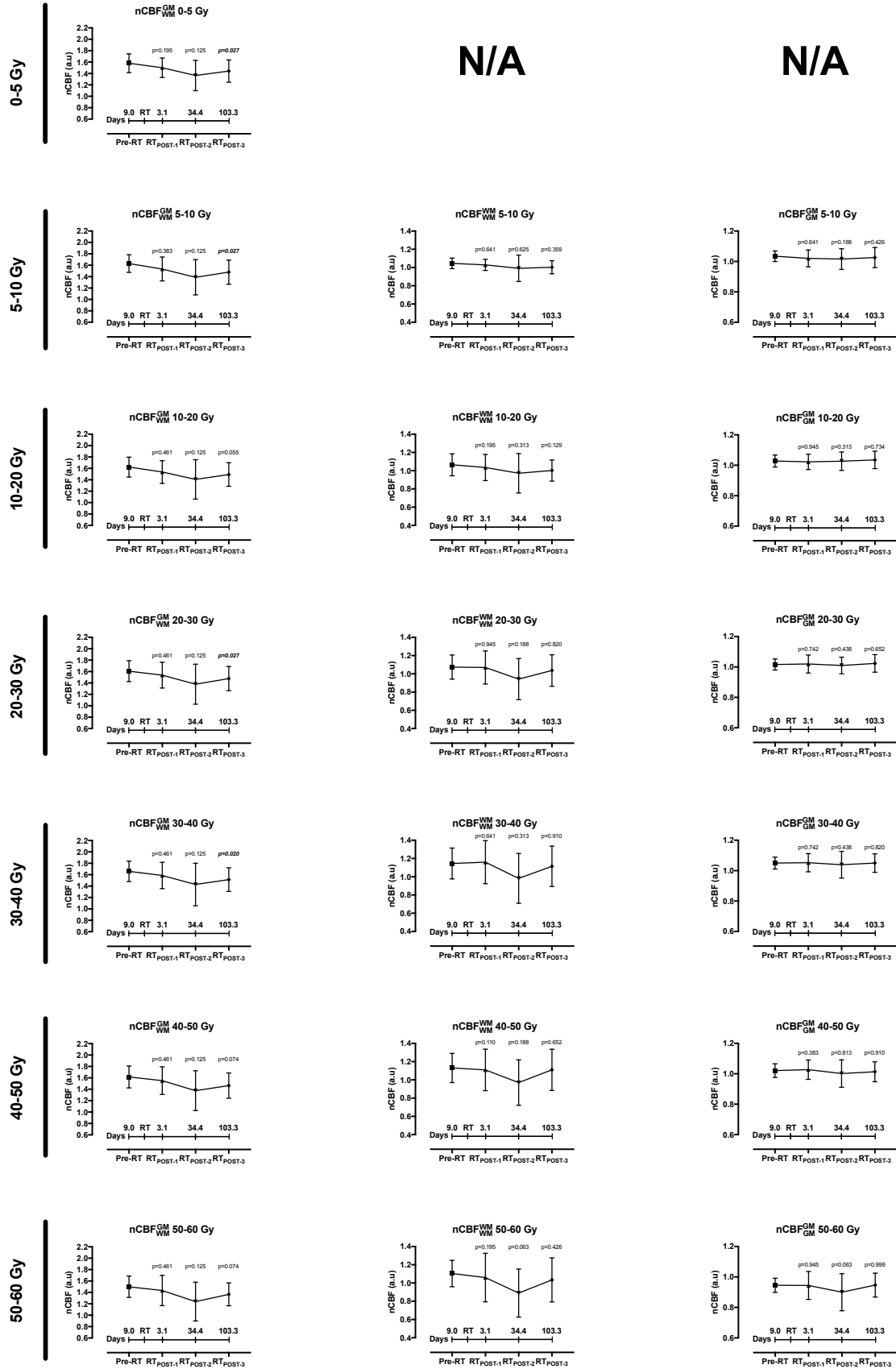
Perfusion magnetic resonance imaging changes in normal appearing brain tissue after radiotherapy in glioblastoma patients may confound longitudinal evaluation of treatment response

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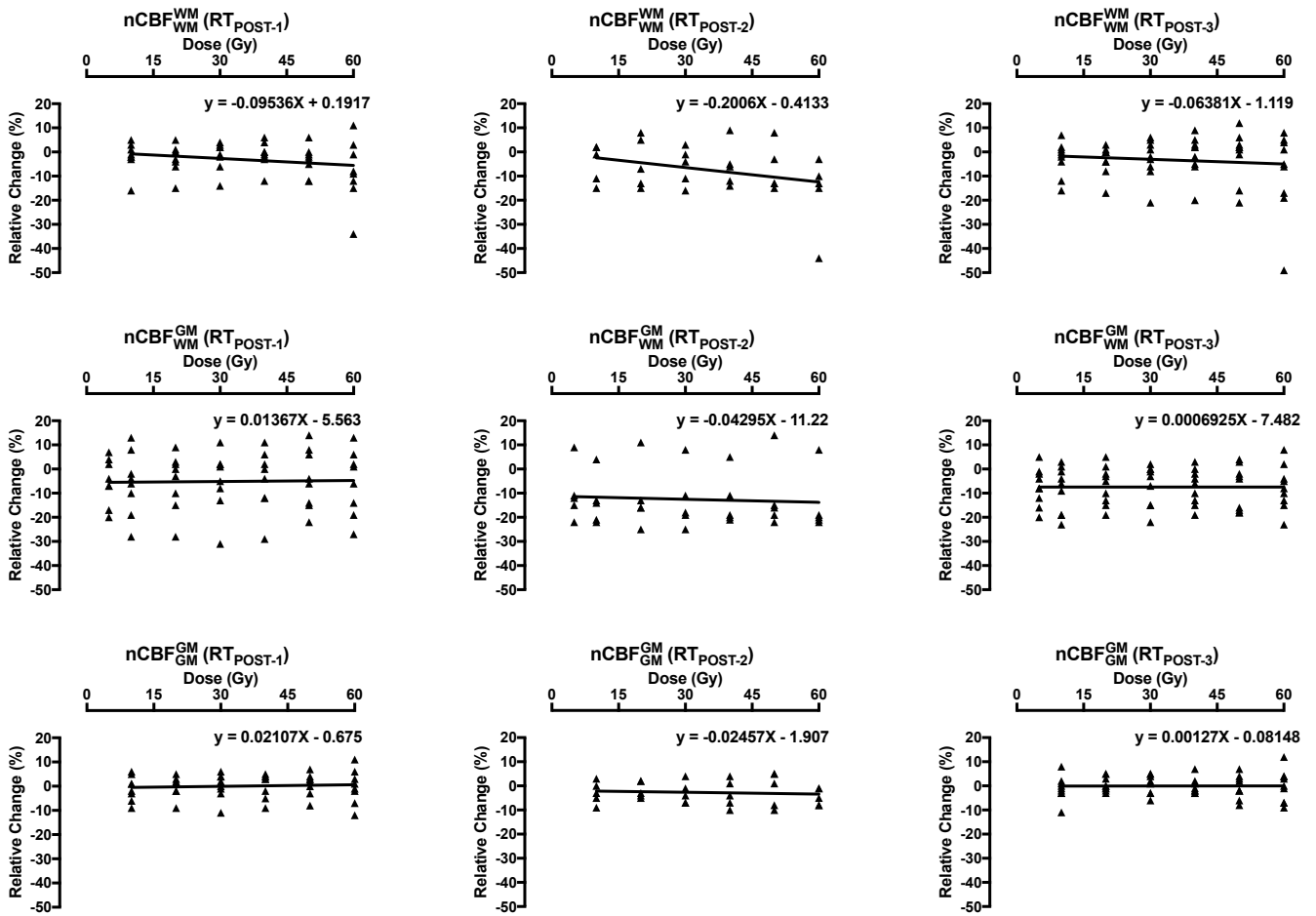
doi: 10.2478/raon-2018-0022



S1 FIGURE. Longitudinal change in regional nCBV. Regional nCBV (mean and 95% CI) graphically displayed for the different examinations in consecutive order. Derived P-values are included, and emphasised in bold and italics if less than 0.05.



52 FIGURE. Longitudinal change in regional nCBF. Regional nCBF (mean and 95% CI) graphically displayed for the different examinations in consecutive order. Derived P-values are included, and emphasised in bold and italics if less than 0.05.



S3 FIGURE. Dose-dependent relative change and linear regression model for nCBF. Shows regional relative change for nCBF and derived line regression (line and equation).

S1 TABLE. Volumes for derived dose regions. Mean volume in cm³ with 95% confident interval for the derived dose regions.

Dose Region	Volume (cm ³) Mean (95% CI)	
	GM	WM
0-5 Gy	84.5 (74.5-94.5)	56.0 (47.1-64.8)
5-10 Gy	36.4 (27.5-45.2)	33.4 (24.3-42.4)
10-20 Gy	62.7 (54.8-70.6)	51.5 (43.5-59.6)
20-30 Gy	91.0 (81.0-101.1)	73.7 (65.1-82.4)
30-40 Gy	35.0 (31.9-38.2)	32.3 (29.0-35.7)
40-50 Gy	28.2 (24.1-34.2)	19.7 (18.2-21.2)
50-60 Gy	117.3 (106.7-127.8)	90.2 (78.4-102.0)

S2 TABLE. Mean and SEM for regional nCBV and nCBF. Regional nCBV and nCBF (mean and SEM), decrease in percentage relative Pre-FRT (mean and SD) and derived P-values.

nCBV ^{GM} _{WM}					nCBV ^{WM} _{WM}					nCBV ^{GM} _{GM}							
	Pre-RT	Post-RT 1	Post-RT 2	Post-RT 3		Pre-RT	Post-RT 1	Post-RT 2	Post-RT 3		Pre-RT	Post-RT 1	Post-RT 2	Post-RT 3			
0-5 Gy	nCBV	1.62 ± 0.07	1.53 ± 0.08	1.37 ± 0.09	1.51 ± 0.08	5-10 Gy	nCBV	1.04 ± 0.03	1.01 ± 0.02	1.04 ± 0.03	1.03 ± 0.03	5-10 Gy	nCBV	1.03 ± 0.02	1.01 ± 0.02	1.03 ± 0.03	1.03 ± 0.03
	ΔnCBV (%)		-6.0 ± 7.3	-6.2 ± 14.7	-5.6 ± 9.1		ΔnCBV (%)		-3.5 ± 7.1	2.0 ± 10.1	0.2 ± 7.7		ΔnCBV (%)		-0.4 ± 3.2	0.0 ± 5.1	-0.2 ± 4.7
	p-value		0,0781	0,4375	0,0742		p-value		0,3125	0,8125	0,6523		p-value		0,8438	0,8125	>0,9999
5-10 Gy	nCBV	1.66 ± 0.07	1.55 ± 0.09	1.50 ± 0.13	1.55 ± 0.09	10-20 Gy	nCBV	1.08 ± 0.05	1.03 ± 0.06	1.03 ± 0.07	1.02 ± 0.05	10-20 Gy	nCBV	1.02 ± 0.03	0.99 ± 0.02	1.03 ± 0.04	1.02 ± 0.04
	ΔnCBV (%)		-6.3 ± 8.5	-6.2 ± 11.0	-5.8 ± 9.2		ΔnCBV (%)		-4.1 ± 7.2	1.2 ± 10.9	-2.9 ± 6.8		ΔnCBV (%)		-1.4 ± 2.1	1.4 ± 3.0	-0.4 ± 8.3
	p-value		0,0781	0,3125	0,2031		p-value		0,1484	>0,9999	0,1289		p-value		0,1094	0,625	0,9102
10-20 Gy	nCBV	1.65 ± 0.08	1.53 ± 0.10	1.52 ± 0.15	1.53 ± 0.08	20-30 Gy	nCBV	1.09 ± 0.06	1.05 ± 0.07	1.03 ± 0.08	1.03 ± 0.07	20-30 Gy	nCBV	1.01 ± 0.03	0.99 ± 0.03	1.03 ± 0.03	1.00 ± 0.04
	ΔnCBV (%)		-7.5 ± 6.7	-4.6 ± 13.7	-6.1 ± 11.5		ΔnCBV (%)		-3.1 ± 7.5	3.0 ± 5.2	-4.2 ± 8.0		ΔnCBV (%)		-1.3 ± 4.4	1.2 ± 5.5	-0.9 ± 8.5
	p-value		0,0234	0,625	0,3008		p-value		0,3125	0,4375	0,3008		p-value		0,4609	0,625	0,9102
20-30 Gy	nCBV	1.64 ± 0.09	1.53 ± 0.11	1.51 ± 0.13	1.51 ± 0.09	30-40 Gy	nCBV	1.14 ± 0.08	1.13 ± 0.09	1.06 ± 0.09	1.09 ± 0.08	30-40 Gy	nCBV	1.03 ± 0.03	1.02 ± 0.04	1.08 ± 0.04	1.03 ± 0.03
	ΔnCBV (%)		-7.3 ± 8.1	-4.8 ± 12.3	-6.6 ± 10.6		ΔnCBV (%)		-2.0 ± 6.3	4.4 ± 8.3	-1.8 ± 11.7		ΔnCBV (%)		-0.8 ± 2.9	4.0 ± 7.6	-0.2 ± 7.9
	p-value		0,0391	0,625	0,2031		p-value		0,4609	0,3125	>0,9999		p-value		0,6406	0,3125	0,4961
30-40 Gy	nCBV	1.68 ± 0.10	1.58 ± 0.12	1.58 ± 0.14	1.55 ± 0.09	40-50 Gy	nCBV	1.13 ± 0.08	1.08 ± 0.09	1.06 ± 0.09	1.10 ± 0.09	40-50 Gy	nCBV	0.99 ± 0.03	0.99 ± 0.03	1.02 ± 0.04	1.00 ± 0.04
	ΔnCBV (%)		-6.8 ± 6.8	-2.0 ± 9.3	-5.8 ± 9.6		ΔnCBV (%)		-3.9 ± 7.0	2.6 ± 10.1	-1.6 ± 11.5		ΔnCBV (%)		0.9 ± 5.1	4.4 ± 7.4	1.0 ± 5.0
	p-value		0,0391	0,8125	0,5703		p-value		0,1484	0,8125	0,8203		p-value		0,6406	0,3125	0,8203
40-50 Gy	nCBV	1.61 ± 0.09	1.53 ± 0.12	1.51 ± 0.15	1.51 ± 0.10	50-60 Gy	nCBV	1.13 ± 0.08	1.05 ± 0.10	0.99 ± 0.13	1.01 ± 0.10	50-60 Gy	nCBV	0.95 ± 0.03	0.92 ± 0.04	0.94 ± 0.05	0.93 ± 0.04
	ΔnCBV (%)		-5.0 ± 7.3	-1.6 ± 11.4	-4.7 ± 7.6		ΔnCBV (%)		-9.1 ± 10.3	-9.2 ± 21.2	-11.7 ± 19.9		ΔnCBV (%)		-2.3 ± 5.8	-0.8 ± 5.4	-1.7 ± 7.0
	p-value		0,0781	>0,9999	0,1289		p-value		0,0391	0,625	0,1641		p-value		0,5469	0,8125	0,8203
50-60 Gy	nCBV	1.54 ± 0.09	1.44 ± 0.12	1.38 ± 0.15	1.40 ± 0.09												
	ΔnCBV (%)		-8.3 ± 11.0	-6.8 ± 15.5	-7.2 ± 10.4												
	p-value		0,1484	0,625	0,0742												

nCBF ^{GM} _{WM}					nCBF ^{WM} _{WM}					nCBF ^{GM} _{GM}							
	Pre-RT	Post-RT 1	Post-RT 2	Post-RT 3		Pre-RT	Post-RT 1	Post-RT 2	Post-RT 3		Pre-RT	Post-RT 1	Post-RT 2	Post-RT 3			
0-5 Gy	nCBF	1.58 ± 0.07	1.50 ± 0.07	1.37 ± 0.10	1.44 ± 0.08	5-10 Gy	nCBF	1.05 ± 0.03	1.03 ± 0.03	0.99 ± 0.05	1.00 ± 0.03	5-10 Gy	nCBF	1.03 ± 0.02	1.02 ± 0.02	1.02 ± 0.02	1.03 ± 0.03
	ΔnCBF (%)		-5.3 ± 9.6	-10.2 ± 11.6	-7.3 ± 7.8		ΔnCBF (%)		-1.9 ± 6.3	-4.6 ± 7.9	-2.8 ± 7.1		ΔnCBF (%)		-0.9 ± 5.2	-2.8 ± 4.6	-1.0 ± 5.1
	p-value		0,1953	0,125	0,0273		p-value		0,6406	0,625	0,3594		p-value		0,6406	0,1875	0,4258
5-10 Gy	nCBF	1.63 ± 0.06	1.54 ± 0.09	1.39 ± 0.11	1.48 ± 0.09	10-20 Gy	nCBF	1.07 ± 0.05	1.04 ± 0.06	0.97 ± 0.08	1.00 ± 0.05	10-20 Gy	nCBF	1.03 ± 0.02	1.02 ± 0.02	1.03 ± 0.02	1.04 ± 0.02
	ΔnCBF (%)		-6.0 ± 13.3	-13.2 ± 10.4	-8.6 ± 9.6		ΔnCBF (%)		-2.8 ± 6.0	-4.4 ± 10.4	-3.2 ± 6.1		ΔnCBF (%)		-0.1 ± 4.3	-1.6 ± 3.4	0.7 ± 3.0
	p-value		0,3828	0,125	0,0273		p-value		0,1953	0,3125	0,1289		p-value		0,9453	0,3125	0,7344
10-20 Gy	nCBF	1.62 ± 0.08	1.54 ± 0.08	1.41 ± 0.12	1.49 ± 0.09	20-30 Gy	nCBF	1.07 ± 0.06	1.07 ± 0.08	0.94 ± 0.08	1.04 ± 0.07	20-30 Gy	nCBF	1.02 ± 0.02	1.02 ± 0.02	1.01 ± 0.02	1.02 ± 0.03
	ΔnCBF (%)		-5.3 ± 11.9	-11.8 ± 13.5	-6.8 ± 7.9		ΔnCBF (%)		-1.5 ± 6.0	-5.8 ± 7.7	-2.8 ± 8.3		ΔnCBF (%)		0.1 ± 5.4	-3.0 ± 4.6	0.7 ± 3.9
	p-value		0,4609	0,125	0,0547		p-value		0,9453	0,1875	0,8203		p-value		0,7422	0,4375	0,6523
20-30 Gy	nCBF	1.61 ± 0.08	1.54 ± 0.10	1.38 ± 0.13	1.48 ± 0.09	30-40 Gy	nCBF	1.15 ± 0.07	1.16 ± 0.10	0.98 ± 0.10	1.12 ± 0.10	30-40 Gy	nCBF	1.05 ± 0.02	1.05 ± 0.03	1.04 ± 0.03	1.05 ± 0.03
	ΔnCBF (%)		-5.1 ± 12.8	-13.0 ± 12.8	-6.8 ± 8.5		ΔnCBF (%)		-1.0 ± 5.4	-5.6 ± 9.0	-1.3 ± 8.5		ΔnCBF (%)		0.4 ± 5.1	-3.2 ± 5.7	0.0 ± 3.2
	p-value		0,4609	0,125	0,0273		p-value		0,6406	0,3125	0,9102		p-value		0,7422	0,4375	0,8203
30-40 Gy	nCBF	1.66 ± 0.08	1.59 ± 0.10	1.43 ± 0.13	1.51 ± 0.09	40-50 Gy	nCBF	1.13 ± 0.07	1.11 ± 0.10	0.97 ± 0.09	1.11 ± 0.10	40-50 Gy	nCBF	1.02 ± 0.02	1.03 ± 0.03	1.00 ± 0.03	1.01 ± 0.03
	ΔnCBF (%)		-4.8 ± 13.2	-13.2 ± 10.9	-7.3 ± 7.4		ΔnCBF (%)		-3.6 ± 6.1	-7.2 ± 9.7	-1.3 ± 8.5		ΔnCBF (%)		1.0 ± 4.7	-1.4 ± 7.2	-0.4 ± 4.9
	p-value		0,4609	0,125	0,0195		p-value		0,1094	0,1875	0,6523		p-value		0,3828	0,8125	0,9102
40-50 Gy	nCBF	1.62 ± 0.08	1.55 ± 0.10	1.38 ± 0.13	1.46 ± 0.10	50-60 Gy	nCBF	1.10 ± 0.06	1.06 ± 0.11	0.89 ± 0.09	1.03 ± 0.10	50-60 Gy	nCBF	0.95 ± 0.02	0.94 ± 0.07	0.90 ± 0.04	0.95 ± 0.03
	ΔnCBF (%)		-4.1 ± 12.6	-11.6 ± 14.6	-7.9 ± 9.3		ΔnCBF (%)		-8.1 ± 13.5	-17.0 ± 15.8	-8.7 ± 17.8		ΔnCBF (%)		-0.1 ± 7.2	-4.6 ± 3.5	-0.1 ± 6.8
	p-value		0,4609	0,125	0,0742		p-value		0,1953	0,0625	0,4258		p-value		0,9453	0,0625	>0,9999
50-60 Gy	nCBF	1.50 ± 0.08	1.43 ± 0.11	1.24 ± 0.12	1.37 ± 0.09												
	ΔnCBF (%)		-5.5 ± 13.6	-14.8 ± 12.8	-7.6 ± 9.2												
	p-value		0,4609	0,125	0,0742												