

# Supplementary Material: Magnetic Resonance with Diffusion and Dynamic Perfusion-Weighted Imaging in the Assessment of Early Chemoradiotherapy Response of Naso-Oropharyngeal Carcinoma

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## Material and Methods

**Table S1.** Patients' data retrieved in the study. M: male; F: female; O: oropharynx; N: nasopharynx; P: positive; N: negative; U: unknown; RT: post-chemoradiotherapy changes; PR: tumour persistence/recurrence. \*The eighth edition of the American Joint Commission on Cancer TNM staging

Patient	Gender	Age in years	Tumour site	HPV status	TNM*	Tumour stage	Follow-up
1	F	63	O	P	T2N1M0	I	RT
2	M	48	N	U	T4N2M0	IVA	RT
3	F	72	O	U	T3N0M0	III	RT
4	M	72	O	P	T2N1M0	I	RT
5	M	61	O	U	T4aN2bM0	IVA	RT
6	F	36	N	U	T2aN1M0	IIB	RT
7	F	52	N	N	T1N0M0	I	PR
8	M	81	O	P	T1N1M0	I	RT
9	M	57	N	N	T1N2M0	III	RT
10	F	58	O	U	T4aN1M0	IVA	RT
11	M	59	N	U	T2bN2M0	III	RT
12	M	68	O	P	T1N1M0	I	RT
13	M	58	O	P	T1N1M0	I	RT
14	F	63	O	P	T2N1M0	I	RT
15	M	75	O	P	T1N1M0	I	RT
16	F	57	O	P	T1N1M0	I	RT

17	M	37	N	U	T2aN3M0	IVB	RT
18	F	51	O	P	T2N1M0	I	RT
19	M	61	O	U	T4aN1M0	IVA	RT
20	M	57	O	P	T2N1M0	I	RT
21	F	52	N	U	T1N1M0	IIB	RT
22	M	67	O	N	T4aN0M0	IVA	RT
23	F	65	O	U	T3N1M0	III	RT
24	M	58	N	U	T3N3M1	IVC	PR
25	F	63	N	N	T4N2M0	IVA	RT
26	F	55	O	U	T4aN1M0	IVA	PR
27	F	47	O	P	T4N1M0	II	RT
28	M	61	O	P	T1N2M0	II	RT
29	F	47	O	N	T4aN2M0	IVA	PR
30	F	69	O	P	T2N1M0	I	RT
31	M	41	O	P	T1N1M0	I	RT
32	M	52	N	U	T2N0M0	IIA	RT
33	F	55	O	P	T1N1M0	I	RT
34	M	63	O	N	T3N1M0	III	PR
35	F	58	N	U	T2N2M0	III	RT
36	F	39	O	P	T2N1M0	I	RT
37	M	56	O	P	T2N1M0	I	RT

**Table S2.** Magnetic resonance acquisition protocol performed for the study of naso-oropharyngeal carcinoma staging and 4-month follow-up from ending chemoradiotherapy. Unenhanced scans included sagittal fat saturated T1- and T2-weighted sampling perfection with application-optimized contrasts using different flip angle evolution (SPACE) sequences with axial, coronal, and sagittal multiplanar reconstructions; axial T2-weighted turbo spin echo; axial fat saturated echo-planar DWI spectral attenuated inversion recovery (SPAIR) with two b-values (b50-800 s/mm<sup>2</sup>) and ADC maps; two axial T1-weighted volumetric interpolated breath-hold examination (VIBE) DCE-PWI with application of flip angle (FA) 5° and 15°, respectively. Enhanced scans performed after intravenous gadolinium chelates contrast agent injection (gadobutrol, 1 mL/10 kg, flow 3 mL/sec followed by 20 mL saline flush) consisted of an axial VIBE DCE-PWI with application of FA 30° and peripheral K space sampling with time to centre 2.2 s, an axial T1-weighted turbo spin echo, and an axial VIBE Dixon.

Sequence	Contrast agent	Repetition time (ms)	Echo time (ms)	Slice thickness (mm)	Interslice gap (mm)	Field of view (mm)	Matrix	Acceleration factor	Number of signal averaged	Band width (Hz/Px)	Acquisition time (min:sec)	Voxel size
SPACE T1-w Sagittal	pre	500	7.2	0.9	-	229 x	230 x	2	1.4	630	5:47	0.9 x 0.9 x 0.9
SPACE T2-w Sagittal Fat-Sat	pre	3000	380	0.9	-	229 x	230 x	2	1.4	698	5:56	0.9 x 0.9 x 0.9
TSE T2-w Axial	pre	5050	117	3	0.9	210 x	261 x	2	3	191	2:23	0.5 x 0.5 x 3.0
SPAIR EPI- DWI Axial (b 50/800 s/mm <sup>2</sup> )	pre	4100	55	3	0.9	240 x	102 x	3	1	1608	3:09	1.6 x 1.6 x 3.0
VIBE T1-w DCE-PWI Axial; FA 5°, 15°	pre	4.65	1.66	3.5	0.7	250 x	139 x	3	1	390	1:04	1.3 x 1.3 x 3.5
TSE T1-w Axial	post	440	17	3	0.9	200 x	384 x	3	3	200	2:31	0.5 x 0.5 x 3.0
VIBE Dixon Axial	post	10	2.4	0.9	0.18	225 x	212 x	-	1	340	4:37	0.9 x 0.9 x 0.9
VIBE T1-w DCE-PWI Axial; FA 30°	post	4.65	1.66	3.5	0.7	250 x	139 x	3	1	300	4:17	1.3 x 1.3 x 3.5

## Results

**Table S3.** Pre-treatment patients' data.

ADC: apparent diffusion coefficient; AUC: area under the curve; k(trans): the volume transfer constant from the vascular space to the extravascular extracellular space; pre: values measured on magnetic resonance imaging performed for tumour staging.

Patient	Tumour maximum size (mm)	Tumour mean ADC ( $\times 10^{-3}$ mm <sup>2</sup> /s) [ADCpre]	Ipsilateral trapezius muscle mean ADC ( $\times 10^{-3}$ mm <sup>2</sup> /s) [ADCmuscle pre]	ADCpre/muscle pre	Tumour mean AUC [AUCpre]	Ipsilateral trapezius muscle mean AUC [AUCmuscle pre]	AUC pre/muscle pre	Tumour mean K(trans) value ( $\times 10^{-3}$ min) [K(trans)pre]	Ipsilateral trapezius muscle mean K(trans) [K(trans)muscle pre]	K(trans) pre/muscle pre
1	15	0.98	1.23	0.79	157.64	35.65	4.42	357.83	46.41	7.71
2	17	0.74	1.23	0.60	58.74	8.97	6.55	78.22	20.20	3.87
3	40	1.13	1.14	0.99	99.44	21.50	4.63	786.30	93.28	8.42
4	13	0.74	1.43	0.51	146.75	27.02	5.43	347.44	48.55	7.71
5	32	0.67	1.24	0.54	57.39	18.31	3.13	726.74	122.06	5.95
6	15	0.73	1.45	0.50	80.81	52.73	1.53	105.12	68.92	1.52
7	30	0.92	1.26	0.73	55.66	17.63	3.16	167.50	39.13	4.28
8	15	1.14	1.23	0.92	83.51	36.02	2.31	493.01	38.97	12.92
9	15	0.56	1.16	0.48	76.38	27.16	2.81	231.07	37.05	5.75
10	20	1.04	1.24	0.83	190.12	38.54	4.93	493.36	115.59	4.26
11	14	0.76	1.13	0.67	70.31	40.85	1.72	354.09	174.07	2.03
12	10	0.93	1.15	0.80	44.71	9.07	4.93	79.71	14.54	5.48
13	18	0.74	1.22	0.60	79.62	18.10	4.39	275.87	44.61	6.18
14	15	0.72	1.13	0.63	78.04	25.02	3.11	92.84	15.65	5.93
15	24	0.64	1.11	0.57	56.36	15.82	3.56	375.88	93.92	4.0
16	14	0.76	1.24	0.61	70.33	35.12	2.01	79.79	40.63	1.96
17	12	0.72	1.24	0.58	49.57	19.47	2.54	141.65	34.56	4.09
18	17	0.86	1.12	0.76	103.94	24.68	4.21	135.98	23.63	5.75
19	20	0.97	1.22	0.79	100.99	15.99	6.73	159.62	13.76	11.60
20	11	0.83	1.34	0.61	213.73	47.41	4.50	331.72	41.46	8.04
21	13	0.65	1.23	0.52	116.34	50.28	2.31	134.07	44.23	3.02
22	20	0.99	1.13	0.87	70.71	12.79	5.52	391.55	37.20	10.52
23	17	0.96	0.95	1.01	147.01	29.03	5.06	269.13	45.89	5.91
24	7	1.0	1.22	0.81	159.7	45.90	3.46	231.28	49.19	4.70
25	21	0.78	1.17	0.66	128.12	68.04	1.88	173.49	74.38	2.33
26	22	0.80	1.23	0.65	90.94	24.12	3.77	113.35	21.67	5.23
27	35	0.79	1.26	0.62	51.80	21.54	2.42	61.39	12.76	4.81
28	17	0.87	1.09	0.79	113.87	35.40	3.21	128.46	32.45	3.95
29	23	0.83	1.16	0.71	100.14	16.98	5.89	117.63	24.86	4.73

30	20	0.74	1.18	0.62	69.72	28.58	2.43	80.56	32.24	2.49
31	14	1.03	1.15	0.89	82.51	35.02	2.35	488.01	39.97	12.20
32	12	0.75	1.20	0.62	78.38	29.16	2.68	230.07	36.05	6.38
33	8	0.94	1.11	0.84	188.22	36.54	5.15	470.36	113.59	4.14
34	23	0.81	1.18	0.68	100.38	17.18	5.84	118.70	25.68	4.62
35	32	0.68	1.20	0.56	71.41	41.35	1.72	355.19	174.57	2.03
36	15	0.90	1.23	0.73	42.71	8.95	4.77	78.81	14.77	5.33
37	17	0.75	1.11	0.67	79.69	18.20	4.37	273.82	44.31	6.17

**Table S4.** Post-treatment patients' data.

T2 signal intensity is referred with respect to the muscle. Hypo: lower than muscle. Hyper+: similar or slightly higher than muscle. Higher ++: clearly higher than muscle; ADC: apparent diffusion coefficient; AUC: area under the curve; K(trans): the volume transfer constant from the vascular space to the extravascular extracellular space; post: values measured on magnetic resonance imaging performed for 4-month follow-up.

Patient	Submucosal enhanced thickness (mm)	T2 signal intensity	DWI b800 signal intensity	Residual tissue mean ADC ( $\times 10^{-3} \text{ mm}^2/\text{s}$ ) [ADCpost]	Ipsilateral trapezius muscle mean ADC ( $\times 10^{-3} \text{ mm}^2/\text{s}$ ) [ADCmuscle post]	ADCpost/muscle post	Residual tissue mean AUC [AUCpost]	Ipsilateral trapezius muscle AUC [AUCmuscle post]	AUCpost/muscle post	Residual tissue mean K(trans) ( $\times 10^{-3} \text{ min}$ ) [K(trans)post]	Ipsilateral trapezius muscle mean K(trans) [K(trans) muscle post]	K(trans) post/muscle post
1	0	Hyper ++	Hypo	1.75	1.23	1.42	89.67	26.87	3.33	176.87	33.21	5.32
2	3	Hyper +	Hypo	1.76	1.32	1.33	35.37	10	3.54	72.4	21.75	3.32
3	10	Hyper +	Hypo	1.60	1.14	1.40	216.24	44.49	4.86	97.82	20.16	4.85
4	0	Hypo	Hypo	1.47	1.25	1.76	61.72	30.2	2.04	31.33	11.33	2.76
5	10	Hypo	Hypo	1.33	1.12	1.18	83.73	29.83	2.8	223.99	115.13	1.94
6	5	Hyper ++	Hyper	1.53	1.32	1.16	88.04	21.38	4.11	595.25	123.07	4.83
7	27	Hyper +	Hyper	1.24	1.62	0.77	59.77	17	3.52	128.1	28.1	4.55
8	0	Hypo	Hypo	1.44	1.12	1.29	188.77	57.9	3.26	422	28.56	14.77
9	6	Hyper ++	Hypo	1.75	1.13	1.55	117.93	19.41	6.07	590.69	25.6	23.07
10	10	Hyper ++	Hyper	1.35	1.23	1.10	96.93	28.33	3.42	77.54	11.8	6.57
11	6	Hyper +	Hypo	1.48	1.22	1.21	51.66	23.35	2.21	87.95	50.84	1.72
12	0	Hyper ++	Hypo	1.34	1.13	1.85	108.56	18.08	6.01	76.41	8.46	9.03
13	9	Hypo	Hypo	1.66	1.32	1.26	63.53	13.99	4.54	787.92	153.73	5.12
14	0	Hypo	Hypo	1.44	1.23	1.17	98.93	51.03	1.93	48.36	26.49	1.82
15	10	Hypo	Hypo	1.65	1.21	1.36	96.45	18.51	5.21	25.54	7.02	3.36
16	0	Hyper ++	Hypo	1.71	1.32	1.30	152.07	50.91	2.98	202.03	55.45	3.64
17	0	Hyper ++	Hypo	1.31	1.35	0.97	94.94	29.88	3.17	121.81	27.22	4.47
18	0	Hypo	Hypo	1.75	1.22	1.43	84.58	28.29	2.98	87.43	26.93	3.24
19	3	Hyper ++	Hypo	1.61	1.37	1.75	123.78	29.15	4.24	122.78	24.54	5.02
20	4	Hyper ++	Hypo	1.96	1.35	1.45	123.66	28.29	4.37	107.65	23.14	4.65
21	0	Hyper +	Hypo	1.32	1.33	0.99	63.5	55.8	1.13	57.69	49.01	1.17

22	0	Hyper ++	Hypo	1.68	1.13	1.49	68.12	19.89	3.42	65.91	14.61	4.51
23	0	Hyper ++	Hypo	1.83	1.23	1.49	124.21	40.89	3.03	139.23	41.63	3.34
24	12	Hyper +	Hyper	0.87	1.05	0.83	161.98	40.89	3.96	169.92	41.57	4.08
25	0	Hyper ++	Hypo	1.11	1.12	0.99	91.76	39.95	2.29	79.22	41.77	1.89
26	7	Hyper +	Hypo	1.32	1.22	1.08	162.90	36.29	4.48	215.45	39.89	5.40
27	10	Hyper +	Hypo	0.96	1.17	0.82	80.58	18.57	4.33	37.29	7.08	5.26
28	0	Hyper ++	Hypo	1.54	1.28	1.20	67.22	28.01	2.39	30.41	11.15	2.27
29	45	Hyper +	Hyper	0.78	1.01	0.77	109.85	20.23	5.43	56.24	10.39	5.41
30	0	Hyper ++	Hypo	1.72	1.21	1.42	260.88	54.36	4.79	361.56	59.11	6.11
31	0	Hypo	Hypo	1.45	1.13	1.28	59.97	17.12	3.50	421.19	28.04	15.02
32	5	Hyper ++	Hypo	1.76	1.14	1.54	189.77	58.9	3.22	582.68	25.41	22.93
33	11	Hyper ++	Hypo	1.34	1.22	1.09	118.01	19.96	5.91	77.94	11.90	6.54
34	42	Hyper +	Hyper	0.79	1.01	0.78	111.83	21.33	5.24	59.27	12.07	4.91
35	7	Hypo	Hypo	1.49	1.23	1.21	51.40	23.31	2.20	87.05	50.04	1.74
36	0	Hyper ++	Hypo	1.44	1.23	1.17	109.03	18.18	5.99	78.43	9.57	8.19
37	8	Hyper ++	Hypo	1.68	1.34	1.25	63.57	14.02	4.53	780.92	150.73	5.18

**Table S5.** Comparison between post-treatment and pre-treatment patients' data.ADC: apparent diffusion coefficient (expressed in  $\times 10^{-3} \text{ mm}^2/\text{s}$ ).

ADCpost-pre: residual tissue mean ADC value - tumour mean ADC value.

ADCpost-pre%: residual tissue mean ADC value - tumour mean ADC value, expressed in percentage calculated as follows:  $\frac{\text{ADCpost-pre} \times 100}{\text{ADCpre}}$ . Negative percentages indicate that ADCpost values are lower than ADCpre.

AUC: area under the curve.

AUCpost/pre: ratio between the residual tissue AUC and tumour AUC values.

AUCpost/pre/muscle: ratio between residual tissue AUC and tumour AUC values, standardized with respect to AUC values of the ipsilateral trapezius muscle.

K(trans): the volume transfer constant from the vascular space to the extravascular extracellular space.

K(trans)post/pre: ratio between the residual tissue K(trans) value and tumour K(trans) value.

K(trans)post/pre/muscle: ratio between the residual tissue K(trans) and tumour K(trans) values, standardized with respect to K(trans) values of the ipsilateral trapezius muscle.

Patient	ADC post-pre	ADC post-pre%	AUC post/pre	AUC post/pre/muscle	K(trans) post/pre	K(trans) post/pre/muscle
1	0.77	77	0.57	0.75	0.49	0.69
2	1.02	134	0.60	0.50	0.92	0.85
3	0.47	40	2.17	1.01	0.12	0.57
4	0.73	100	0.42	0.37	0.09	0.35
5	0.66	100	1.45	0.93	0.30	0.32
6	0.80	110	1.08	2.70	5.66	3.17
7	0.32	35	1.07	1.10	0.76	1.06
8	0.30	27	2.26	1.41	0.85	1.14
9	1.19	209	1.53	2.20	2.55	4.01
10	0.31	31	0.51	0.72	0.15	1.53
11	0.72	96	0.73	1.30	0.24	0.85
12	0.41	43	2.42	1.23	0.95	1.64
13	0.92	124	0.79	1.03	2.85	0.82

14	0.72	100	1.27	0.61	0.52	0.30
15	1.01	159	1.71	1.47	0.06	0.84
16	0.95	125	2.16	1.55	2.53	1.85
17	0.59	82	1.91	1.24	0.85	1.09
18	0.89	103	0.81	0.75	0.56	0.56
19	0.64	66	1.22	0.63	0.76	0.43
20	1.13	136	0.57	1.09	0.32	0.58
21	0.67	103	0.54	0.52	0.43	0.38
22	0.69	70	0.96	0.61	0.16	0.42
23	0.87	90	0.84	0.60	0.51	0.56
24	-0.13	-13	1.01	1.14	0.73	0.86
25	0.33	42	0.71	1.21	0.45	0.81
26	0.52	65	1.79	1.18	1.90	1.03
27	0.16	21	1.55	1.79	0.60	1.09
28	0.67	76	0.59	0.74	0.23	0.57
29	-0.04	-5	1.09	0.92	0.47	1.14
30	0.98	131	3.74	1.97	4.48	2.44
31	0.43	41	0.73	1.49	0.86	2.44
32	1.01	134	2.42	1.20	2.53	3.59
33	0.40	42	0.63	1.15	0.16	1.57
34	-0.01	-1	1.11	0.90	0.49	1.06
35	0.81	118	0.72	1.28	0.24	0.85
36	0.54	60	2.55	1.25	0.99	1.53
37	0.93	123	0.80	1.04	2.85	0.83