Supplementary Materials

Comprehensive brain tumour characterization with VERDICT-MRI: evaluation of cellular and vascular measures validated by histology

Supplementary Table S1: List of the considered compartment models with the associated parameters and constraints.

| Compartment	Model	Parameters	Constraints
Extracellular (fraction **fees**)	**Zeppelin**	Main orientation: θ, ϕ	None
		Diffusivity along the main axis: $D_{\parallel}$	$1 \cdot 10^{-11}$ m²/s ≤ $D_{\parallel}$ ≤ $3 \cdot 10^{-9}$ m²/s
		Diffusivity in the orthogonal plane: $D_{\perp}$	$1 \cdot 10^{-11}$ m²/s ≤ $D_{\perp}$ ≤ $3 \cdot 10^{-9}$ m²/s $D_{\perp}$ ≤ $D_{\parallel}$
	Tensor	Main orientation: θ, ϕ	None
		Diffusivity along the main axis: $D_{\parallel}$	$1 \cdot 10^{-11}$ m²/s ≤ $D_{\parallel}$ ≤ $3 \cdot 10^{-9}$ m²/s
		Diffusivity in the 1st orthogonal direction: $D_{\perp 1}$	$1 \cdot 10^{-11}$ m²/s ≤ $D_{\perp 1}$ ≤ $3 \cdot 10^{-9}$ m²/s $D_{\perp 1}$ ≤ $D_{\parallel}$
		Diffusivity in the 2nd orthogonal direction: $D_{\perp 2}$	$1 \cdot 10^{-11}$ m²/s ≤ $D_{\perp 2}$ ≤ $3 \cdot 10^{-9}$ m²/s $D_{\perp 2}$ ≤ $D_{\perp 1}$
	Stick	Main orientation: θ, ϕ	None
		Diffusivity along the main axis: $D_{\parallel}$	$1 \cdot 10^{-11}$ m²/s ≤ $D_{\parallel}$ ≤ $3 \cdot 10^{-9}$ m²/s
	WatsonSticks	Main orientation: θ, ϕ	None
		Intrinsic diffusivity: Dees	$1 \cdot 10^{-11}$ m²/s ≤ Dees ≤ $3 \cdot 10^{-9}$ m²/s
		Orientation dispersion: ODI	None
	Cylinder	Main orientation: θ, ϕ	None
		Intrinsic diffusivity: Dees	$1 \cdot 10^{-11}$ m²/s ≤ Dees ≤ $3 \cdot 10^{-9}$ m²/s
		Radius: R_{cyl}	$1 \cdot 10^{-7}$ m ≤ R_{cyl} ≤ $2 \cdot 10^{-5}$ m
Vascular (fraction **fvasc**)	**Ball**	Pseudo-diffusivity: dv	$3 \cdot 10^{-9}$ m²/s ≤ dv ≤ $1 \cdot 10^{-7}$ m²/s or dv fixed to $1.5 \cdot 10^{-8}$ m²/s
	AstroSticks	Pseudo-diffusivity: dv	$9 \cdot 10^{-9}$ m²/s ≤ dv ≤ $1 \cdot 10^{-7}$ m²/s or dv fixed to $4 \cdot 10^{-8}$ m²/s
Intracellular (fraction **fic**)	**Sphere**	Radius: R_{Sph}	$1 \cdot 10^{-7}$ m ≤ R_{Sph} ≤ $2 \cdot 10^{-5}$ m
		Intrinsic diffusivity: Dic	$1 \cdot 10^{-11}$ m²/s ≤ Dic ≤ $3 \cdot 10^{-9}$ m²/s
Free Water (fraction **ffw**)	**Ball**	Diffusivity: D_{FW}	D_{FW} fixed to $3 \cdot 10^{-9}$ m²/s

Supplementary Table S2: Details of patients' characteristics.

| Patient no.	Age	Sex	Biopsy/surgery	Histology diagnosis	WHO grade	IDH mutation
01	69	F	Biopsy	Astrocytoma	3	wild-type
02	61	M	Surgery	Astrocytoma	3	wild-type
03	65	M	Biopsy	Glioblastoma	4	wild-type
04	71	M	Surgery	Melanoma metastasis	/	-
05	41	M	Biopsy	Astrocytoma	3	mutated
06	24	M	Surgery	Astrocytoma	2	wild-type
07	57	M	Surgery	RNa (Pulmonary AdenoCa Met)	/	/
08	74	M	Surgery	Glioblastoma	4	wild-type
09	73	M	Surgery	Astrocytoma	2	wild-type
10	20	M	Surgery	Ependymoma	3	/
11	31	F	Biopsy	Astrocytoma	2 (3)b	wild-type
12	58	M	Biopsy	Glioblastoma	4	wild-type
13	77	M	Surgery	Glioblastoma	4	wild-type
14	65	M	Surgery	Melanoma metastasis	/	/
15	32	F	Surgery	Subependymoma	1	/
16	51	M	Surgery	Astrocytoma	3	mutated
17	65	M	Surgery	Glioblastoma	4	wild-type
18	64	F	Surgery	Astrocytoma	3	mutated
19	19	M	Surgery	Astrocytoma	2	mutated
20	42	M	Surgery	Focal cortical dysplasia	-	-
21	37	F	Surgery	Astrocytoma	2	wild-type

[a] RN = radionecrosis
[b] biopsy-confirmed WHO 2 with foci of radiological progression

Supplementary Table S3: Ranking of two- and three-compartment models fitted on high-b signals, based on the average AICc across patients. A single-Ball model is also included for comparison.

Model ranking in the tumour core	Model ranking in the peritumoural ROI
Zeppelin-Sphere	Zeppelin-Tensor-Sphere
Zeppelin-Cylinder-Sphere	Tensor-Sphere
Zeppelin-Tensor-Sphere	Ball-Tensor-Sphere
Zeppelin-Stick-Sphere	Zeppelin-Cylinder-Sphere
Zeppelin-WatsonSticks-Sphere	Zeppelin-Stick-Sphere
Tensor-Sphere	Zeppelin-Sphere
Ball-Tensor-Sphere	Zeppelin-WatsonSticks-Sphere
Ball-Stick-Sphere	Ball-WatsonSticks-Sphere
Ball-Zeppelin-Sphere	Ball-Zeppelin-Sphere
Ball-WatsonSticks-Sphere	Ball-Stick-Sphere
Ball-Cylinder-Sphere	Ball-Cylinder-Sphere
Ball-Sphere	Ball-Sphere
Cylinder-Sphere	Cylinder-Sphere
Ball	Ball
Stick-Sphere	Stick-Sphere
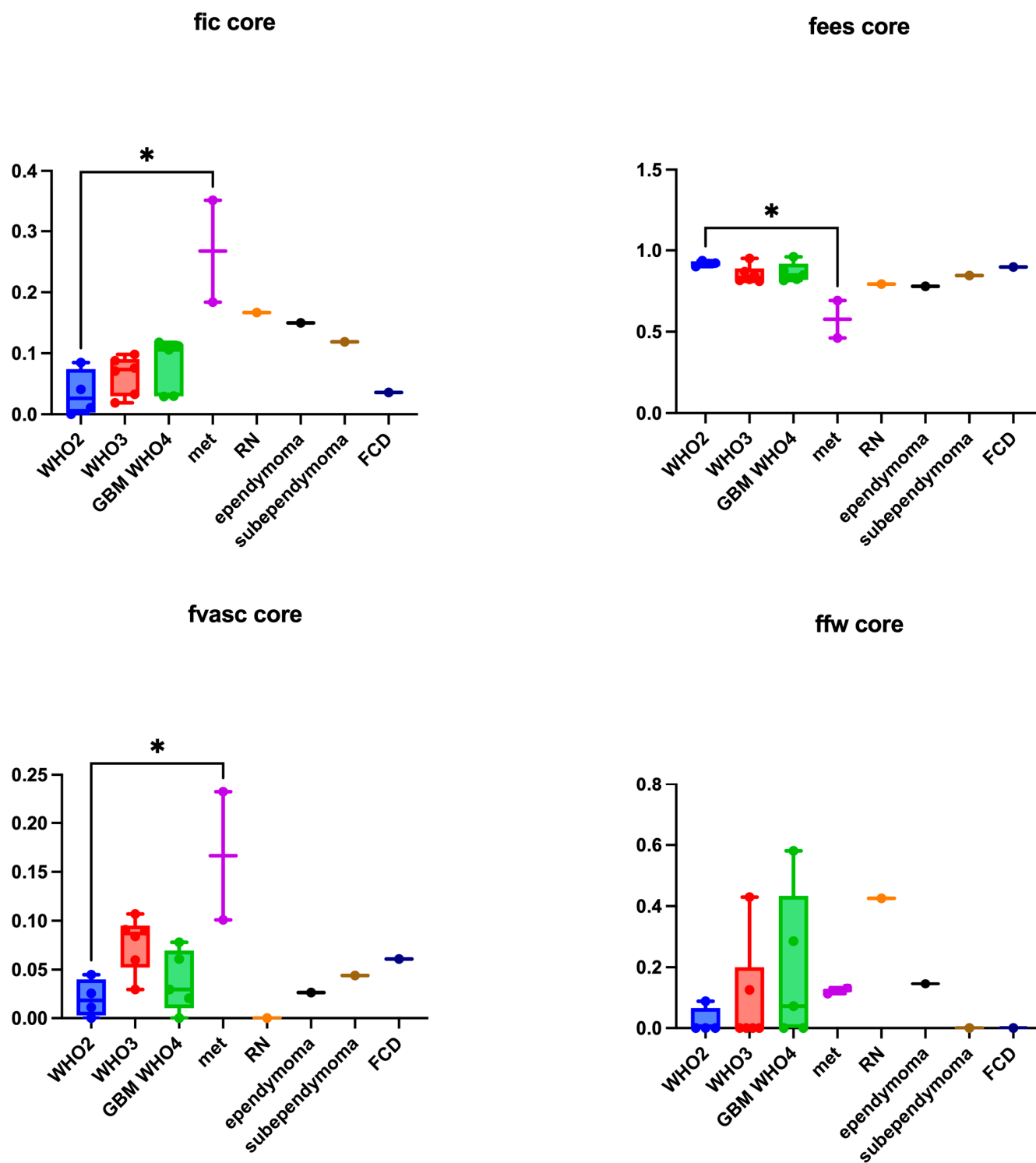
Supplementary Figure S1. VERDICT results in the tumour core for the whole cohort of patients. The boxplots show the ROI median values in each patients group for the signal fraction of each compartment. Statistically significant differences are marked (* p< 0.05).
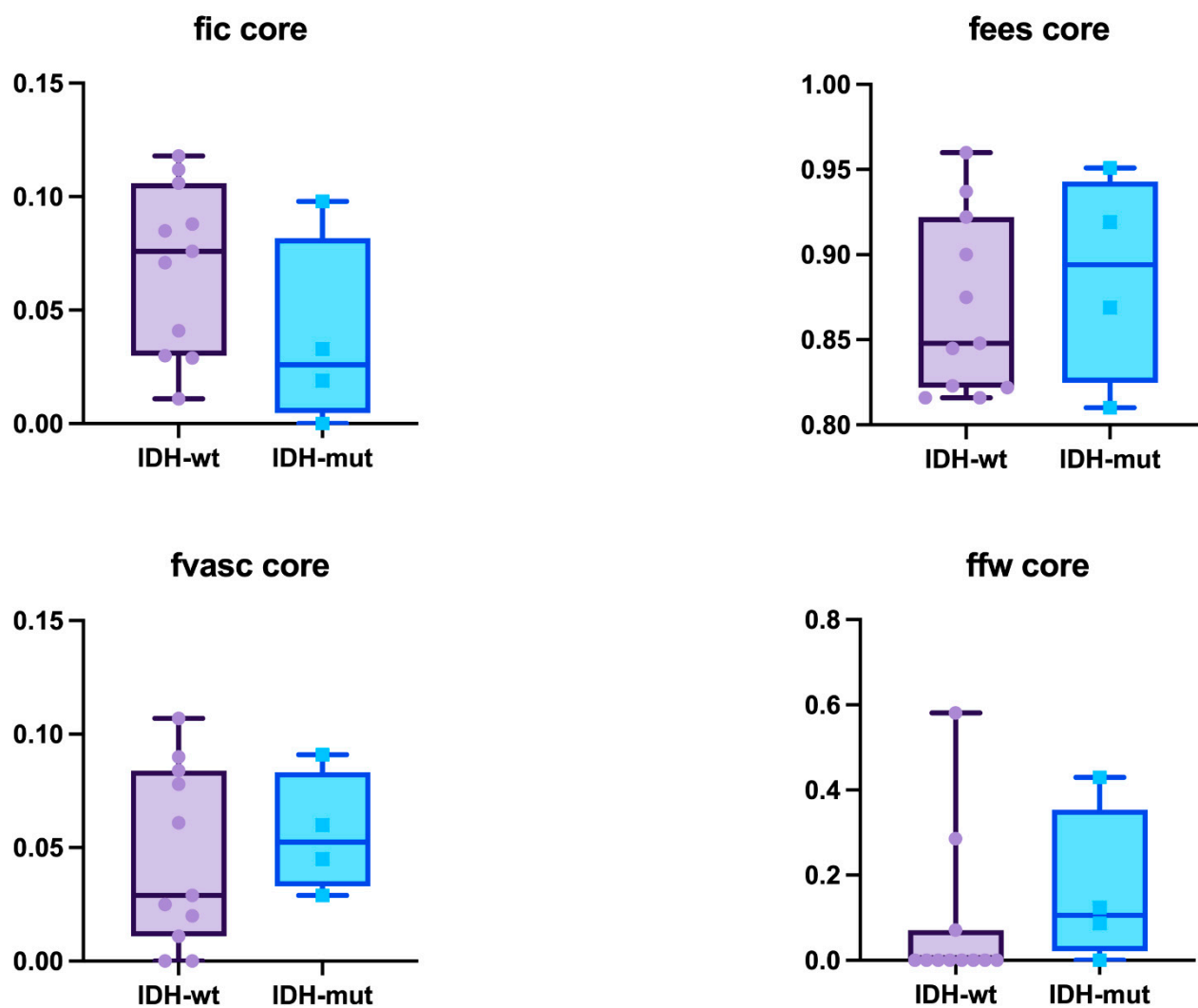
Supplementary Figure S2. VERDICT results in the tumour core according to IDH status. The boxplots show the ROI median values in each patients group for the signal fraction of each compartment.