Supplementary information

**Lesion location implemented magnetic resonance imaging radiomics for predicting *IDH* and *TERT* promoter mutations in grade II/III gliomas**

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**Supplementary Materials**

Table S1. Measured parameters for radiomics.

Table S2. R source codes for Lasso regression.

Table S3. Statistical analysis of measured radiomics parameters.

Fig. S1. Location mapping on MNI152 in the axial plane.

Fig. S2. Location mapping on MNI152 in the coronal plane.

Fig. S3. Location mapping on MNI152 in the sagittal plane.

Fig. S4. Random permutation analysis mapping in the axial plane.

**Table S1**

| Radiomic designation code | Contents of values |
|---|---|
| Histogram and texture parameters | |
| T2_Mean | Mean of VOI in 256-leveled T2-weighted image. |
| T2_SD | Standard deviation of VOI in 256-leveled T2-weighted image. |
| T2_Max | Maximum of VOI in 256-leveled T2-weighted image. |
| T2_Min | Minimum of VOI in 256-leveled T2-weighted image. |
| T2_Median | Median of VOI in 256-leveled T2-weighted image. |
| T2_Mode | Mode of VOI in 256-leveled T2-weighted image. |
| T2_Entropy | Entropy[1)] of VOI in 256-leveled T2-weighted image. |
| T2Edge_Mean | Mean of the rim of VOI in Prewitt filtered[2)] 256-leveled T2-weighted image. |
| T2Edge_SD | Standard deviation of the rim of VOI in Prewitt filtered[2)] 256-leveled T2-weighted image. |
| T2Edge_Max | Maximum of the rim of VOI in Prewitt filtered[2)] 256-leveled T2-weighted image. |
| T2Edge_Min | Minimum of the rim of VOI in Prewitt filtered[2)] 256-leveled T2-weighted image. |
| T2Edge_Median | Median of the rim of VOI in Prewitt filtered[2)] 256-leveled T2-weighted image. |
| T2Edge_Mode | Mode of the rim of VOI in Prewitt filtered[2)] 256-leveled T2-weighted image. |
| T2Edge_Entropy | Entropy[1)] of the rim of VOI in Prewitt filtered[2)] 256-leveled T2-weighted image. |
| T1_Mean | Mean of VOI in 256-leveled T1-weighted image. |
| T1_SD | Standard deviation of VOI in 256-leveled T1-weighted image. |
| T1_Max | Maximum of VOI in 256-leveled T1-weighted image. |
| T1_Min | Minimum of VOI in 256-leveled T1-weighted image. |
| T1_Median | Median of VOI in 256-leveled T1-weighted image. |
| T1_Mode | Mode of VOI in 256-leveled T1-weighted image. |
| T1_Entropy | Entropy[1)] of VOI in 256-leveled T1-weighted image. |
| T1Gd_Mean | Mean of VOI in 256-leveled Gadolinium enhanced T1-weighted image. |

| | |
|---|---|
| T1Gd_SD | Standard deviation of VOI in 256-leveled Gadolinium enhanced T1-weighted image. |
| T1Gd_Max | Maximum of VOI in 256-leveled Gadolinium enhanced T1-weighted image. |
| T1Gd_Min | Minimum of VOI in 256-leveled Gadolinium enhanced T1-weighted image. |
| T1Gd_Median | Median of VOI in 256-leveled Gadolinium enhanced T1-weighted image. |
| T1Gd_Mode | Mode of VOI in 256-leveled Gadolinium enhanced T1-weighted image. |
| T1Gd_Entropy | Entropy[1)] of VOI in 256-leveled Gadolinium enhanced T1-weighted image. |
| Gdzscore_Mean | Mean of VOI in Gdzscore[3)] image. |
| Gdzscore_SD | Standard deviation of VOI in Gdzscore[3)] image. |
| Gdzscore_Max | Maximum of VOI in Gdzscore[3)] image. |
| Gdzscore_Min | Minimum of VOI in Gdzscore[3)] image. |
| Gdzscore_Median | Median of VOI in Gdzscore[3)] image. |
| Gdzscore_Mode | Mode of VOI in Gdzscore[3)] image. |
| Gdzscore_Entropy | Entropy[1)] of VOI in Gdzscore[3)] image. |
| Gdzscore_area_of_Gd | Ratio of volume with Gdzscore>2.0 within the VOI. |
| FLAIR_Mean | Mean of VOI in 256-leveled FLAIR. |
| FLAIR_SD | Standard deviation of VOI in 256-leveled FLAIR. |
| FLAIR_Max | Maximum of VOI in 256-leveled FLAIR. |
| FLAIR_Min | Minimum of VOI in 256-leveled FLAIR. |
| FLAIR_Median | Median of VOI in 256-leveled FLAIR. |
| FLAIR_Mode | Mode of VOI in 256-leveled FLAIR. |
| FLAIR_Entropy | Entropy[1)] of VOI in 256-leveled FLAIR. |
| Shape related parameters | |
| totalsurfarea | Total surface area ($A$) of the VOI. |
| totalvol | Total volume ($V$) of the VOI. |
| compactness01 | Value calculated by the following equation; $compactness1 = \frac{V}{\sqrt{\pi} * A^{\frac{2}{3}}}$ |
| compactness02 | Value calculated by the following equation; $compactness2 = 36\pi \frac{A^2}{V^3}$ |
| spherical_disproportion | Value calculated by the following equation; $spherical\_disproportion = \frac{A}{4\pi * R^2} = \frac{A}{(6\sqrt{\pi} * V)^{\frac{2}{3}}}$ |
| sphericity | Value calculated by the following equation; $sphericity = \frac{(6\pi^2 V)^{\frac{2}{3}}}{A}$ |
| surface_volume_ratio | Value calculated by the following equation; |

| | |
|---|---|
| | $surface\_volume\_ratio = \frac{A}{V}$ |
| Location related parameters | |
| MNI_str_loc.01 | Occupancy rate of area “0” of the MNI structural atlas within the VOI. This area represents white matter. |
| MNI_str_loc.02 | Occupancy rate of area “1” of the MNI structural atlas within the VOI. This area represents lateral ventricles. |
| MNI_str_loc.03 | Occupancy rate of area “2” of the MNI structural atlas within the VOI. This area represents the cerebrum. |
| MNI_str_loc.04 | Occupancy rate of area “3” of the MNI structural atlas within the VOI. This area represents the frontal lobe. |
| MNI_str_loc.05 | Occupancy rate of area “4” of the MNI structural atlas within the VOI. This area represents the insular lobe. |
| MNI_str_loc.06 | Occupancy rate of area “5” of the MNI structural atlas within the VOI. This area represents the occipital lobe. |
| MNI_str_loc.07 | Occupancy rate of area “6” of the MNI structural atlas within the VOI. This area represents the parietal lobe. |
| MNI_str_loc.08 | Occupancy rate of area “7” of the MNI structural atlas within the VOI. This area represents the basal ganglia. |
| MNI_str_loc.09 | Occupancy rate of area “8” of the MNI structural atlas within the VOI. This area represents the temporal lobe. |
| MNI_str_loc.10 | Occupancy rate of area “8” of the MNI structural atlas within the VOI. This area represents the thalamus. |
| HrvdOxf_loc.01 | Occupancy rate of area “0” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.02 | Occupancy rate of area “1” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.03 | Occupancy rate of area “2” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.04 | Occupancy rate of area “3” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.05 | Occupancy rate of area “4” of the Harvard-Oxford cortical and structural atlas within the VOI. |

| | |
|---|---|
| HrvdOxf_loc.06 | Occupancy rate of area “5” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.07 | Occupancy rate of area “6” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.08 | Occupancy rate of area “7” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.09 | Occupancy rate of area “8” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.10 | Occupancy rate of area “9” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.11 | Occupancy rate of area “10” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.12 | Occupancy rate of area “11” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.13 | Occupancy rate of area “12” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.14 | Occupancy rate of area “13” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.15 | Occupancy rate of area “14” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.16 | Occupancy rate of area “15” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.17 | Occupancy rate of area “16” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.18 | Occupancy rate of area “17” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.19 | Occupancy rate of area “18” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.20 | Occupancy rate of area “19” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.21 | Occupancy rate of area “20” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.22 | Occupancy rate of area “21” of the Harvard-Oxford cortical and structural atlas within the VOI. |

| | |
|---|---|
| HrvdOxf_loc.23 | Occupancy rate of area “22” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.24 | Occupancy rate of area “23” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.25 | Occupancy rate of area “24” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.26 | Occupancy rate of area “25” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.27 | Occupancy rate of area “26” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.28 | Occupancy rate of area “27” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.29 | Occupancy rate of area “28” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.30 | Occupancy rate of area “29” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.31 | Occupancy rate of area “30” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.32 | Occupancy rate of area “31” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.33 | Occupancy rate of area “32” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.34 | Occupancy rate of area “33” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.35 | Occupancy rate of area “34” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.36 | Occupancy rate of area “35” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.37 | Occupancy rate of area “36” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.38 | Occupancy rate of area “37” of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.39 | Occupancy rate of area “38” of the Harvard-Oxford cortical and structural atlas within the VOI. |

| | |
|---|---|
| HrvdOxf_loc.40 | Occupancy rate of area "39" of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.41 | Occupancy rate of area "40" of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.42 | Occupancy rate of area "41" of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.43 | Occupancy rate of area "42" of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.44 | Occupancy rate of area "43" of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.45 | Occupancy rate of area "44" of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.46 | Occupancy rate of area "45" of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.47 | Occupancy rate of area "46" of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.48 | Occupancy rate of area "47" of the Harvard-Oxford cortical and structural atlas within the VOI. |
| HrvdOxf_loc.49 | Occupancy rate of area "48" of the Harvard-Oxford cortical and structural atlas within the VOI. |

1) Entropy($S$) is calculated by the following equation where $p_i$ stands for the frequency of the gray scale level $i$.

$$S = -\sum_{i=0}^{255} p_i \log_2 p_i$$

2) Prewitt filtering was performed by applying first order horizontal Gx and vertical Gy differentiation and by calculating the magnitude G, where Gx and Gy stands for the horizontal and vertical gradient of the image respectively and A for the original two-dimensional gray scale image

$$\mathrm{G}x = \begin{bmatrix} -1 & 0 & +1 \\ -1 & 0 & +1 \\ -1 & 0 & +1 \end{bmatrix} * \mathrm{A}, \quad \mathrm{G}y = \begin{bmatrix} -1 & -1 & -1 \\ 0 & 0 & 0 \\ +1 & +1 & +1 \end{bmatrix} * \mathrm{A}, \quad \mathrm{G} = \sqrt{\mathrm{G}x^2 + \mathrm{G}y^2}$$

3) Gdzscore image was created by visualizing the magnitude of enhancement calculated from both 256-leveled non-enhanced

and Gadolinium-enhanced T1-weighted images. 256-leveled Gadolinium-enhanced T1-weighted images was plotted as a function of 256-leveled non-enhanced T1-weighted images in whole brain. Linear regression fitting was applied to the data obtained, which can be expressed as follows;

$$(GdT1WI) = \alpha(T1WI) + \beta$$

where ($GdT1WI$) and ($T1WI$) are 256-leveled Gadolinium-enhanced and non-enhanced T1-weighted images. By solving $\alpha$ and $\beta$, one can now determine the linear correlation of 256-leveled Gadolinium-enhanced and non-enhanced T1-weighted images.

Next, the magnitude of deviation from the above solved linear regression line for any particular voxel ($i$) can be expressed as follows:

$$deviation_i = \frac{(GdT1WI)_i - \alpha(T1WI)_i - \beta}{\sqrt{\alpha^2 + 1}}$$

where $(GdT1WI)_i$ and $(T1WI)_i$ are the 256-leved values of voxel ($i$) in Gadolinium-enhanced and non-enhanced T1-weighted images.

Finally, the Gdzscore of each data point was defined as follows

$$Gdzscore_i = \frac{deviation_i - \mu}{\rho}$$

where $\mu$ and $\sigma$ are the means and standard deviation of $deviation_i$ in the whole brain.

**Table S2**

| R code for IDH mutation with location information |
|---|
| ```library(glmnet)``` |

```
library(glmnet)

##### data set prepare for training and validation#####
dataset00 = read.csv("dataset171101Train.csv")
dataset01 = read.csv("dataset171101Validation.csv")

outvar = "IDH.1"
dataset00[,"IDH.1"] = as.factor(paste0("group0",
dataset00[,"IDH.1"]))
dataset01[,"IDH.1"] = as.factor(paste0("group0",
dataset01[,"IDH.1"]))
table(dataset00[,"IDH.1"])
table(dataset01[,"IDH.1"])

modalities = c("T2", "T2E", "T1", "T1Gd", "Gdzscore", "FLAIR")
measures = c("Mean", "SD", "Max", "Min", "Median", "Mode",
"Entropy")
features = c(paste(rep(modalities, each=length(measures)),
measures, sep="_"), "Gdzscore_ara.of.Gd.")
Locations = paste0("Location.", 1:10)
others = c("totalsurfarea", "totalvol", "compactness01",
"compactness02", "sphericalDisproportion", "sphericity",
"surface2volumeratio")
Harvards = paste0("Harvard_", sprintf("%02d", 1:49))

allvars = c(outvar, features, Locations, Harvards, others)

tmpdataset2 = dataset00[,allvars]
tmpdataset2 = subset(tmpdataset2, complete.cases(tmpdataset2))
trainx <- as.matrix((tmpdataset2[,-1]))
trainy <- tmpdataset2[,1]

valdataset2 = dataset01[,allvars]
valdataset2 = subset(valdataset2, complete.cases(valdataset2))
validationx <- as.matrix((valdataset2[,-1]))
validationy <- valdataset2[,1]

paste("complete cases for training N =", nrow(tmpdataset2))
paste("complete cases for validation N =", nrow(valdataset2))


##### lasso regression #####
cvfit <- cv.glmnet(trainx, trainy, family="multinomial",
type.multinomial="grouped")
predytrain <- predict(cvfit, newx=trainx, type="class", s =
'lambda.min')
table(predytrain,trainy)
predyvalidation <- predict(cvfit, newx=validationx,
type="class", s = 'lambda.min')
table(predyvalidation,validationy)
plot(cvfit)
coef(cvfit, s=cvfit$lambda.1se)
```

**R code for IDH mutation without location information**

```
library(glmnet)

##### data set prepare for training and validation#####
dataset00 = read.csv("dataset171101Train.csv")
dataset01 = read.csv("dataset171101Validation.csv")
```

```
outvar = "IDH.1"
dataset00[,"IDH.1"] = as.factor(paste0("group0",
dataset00[,"IDH.1"]))
dataset01[,"IDH.1"] = as.factor(paste0("group0",
dataset01[,"IDH.1"]))
table(dataset00[,"IDH.1"])
table(dataset01[,"IDH.1"])

modalities = c("T2", "T2E", "T1", "T1Gd", "Gdzscore", "FLAIR")
measures = c("Mean", "SD", "Max", "Min", "Median", "Mode",
"Entropy")
features = c(paste(rep(modalities, each=length(measures)),
measures, sep="_"), "Gdzscore_ara.of.Gd.")
Locations = paste0("Location.", 1:10)
others = c("totalsurfarea", "totalvol", "compactness01",
"compactness02", "sphericalDisproportion", "sphericity",
"surface2volumeratio")
Harvards = paste0("Harvard_", sprintf("%02d", 1:49))

allvars = c(outvar, features, others)

tmpdataset2 = dataset00[,allvars]
tmpdataset2 = subset(tmpdataset2, complete.cases(tmpdataset2))
trainx <- as.matrix((tmpdataset2[,-1]))
trainy <- tmpdataset2[,1]

valdataset2 = dataset01[,allvars]
valdataset2 = subset(valdataset2, complete.cases(valdataset2))
validationx <- as.matrix((valdataset2[,-1]))
validationy <- valdataset2[,1]

paste("complete cases for training N =", nrow(tmpdataset2))
paste("complete cases for validation N =", nrow(valdataset2))


##### lasso regression #####
cvfit <- cv.glmnet(trainx, trainy, family="multinomial",
type.multinomial="grouped")
predytrain <- predict(cvfit, newx=trainx, type="class", s =
'lambda.min')
table(predytrain,trainy)
predyvalidation <- predict(cvfit, newx=validationx,
type="class", s = 'lambda.min')
table(predyvalidation,validationy)
plot(cvfit)
coef(cvfit, s=cvfit$lambda.min)
cvfit$lambda.min
```

R code for 3 group discrimination

```
library(glmnet)

##### data set prepare for training and validation#####
dataset00 = read.csv("dataset171101Train.csv")
dataset01 = read.csv("dataset171101Validation.csv")

outvar = "X3.Groups"
dataset00[,"X3.Groups"] = as.factor(paste0("group0",
dataset00[,"X3.Groups"]))
dataset01[,"X3.Groups"] = as.factor(paste0("group0",
dataset01[,"X3.Groups"]))
table(dataset00[,"X3.Groups"])
table(dataset01[,"X3.Groups"])
```

```
modalities = c("T2", "T2E", "T1", "T1Gd", "Gdzscore", "FLAIR")
measures = c("Mean", "SD", "Max", "Min", "Median", "Mode",
"Entropy")
features = c(paste(rep(modalities, each=length(measures)),
measures, sep="_"), "Gdzscore_ara.of.Gd.")
Locations = paste0("Location.", 1:10)
others = c("totalsurfarea", "totalvol", "compactness01",
"compactness02", "sphericalDisproportion", "sphericity",
"surface2volumeratio")
Harvards = paste0("Harvard_", sprintf("%02d", 1:49))

allvars = c(outvar, features, Locations, Harvards, others)

tmpdataset2 = dataset00[,allvars]
tmpdataset2 = subset(tmpdataset2, complete.cases(tmpdataset2))
trainx <- as.matrix((tmpdataset2[,-1]))
trainy <- tmpdataset2[,1]

valdataset2 = dataset01[,allvars]
valdataset2 = subset(valdataset2, complete.cases(valdataset2))
validationx <- as.matrix((valdataset2[,-1]))
validationy <- valdataset2[,1]

paste("complete cases for training N =", nrow(tmpdataset2))
paste("complete cases for validation N =", nrow(valdataset2))


##### lasso regression #####
cvfit <- cv.glmnet(trainx, trainy, family="multinomial",
type.multinomial="grouped")
predytrain <- predict(cvfit, newx=trainx, type="class", s =
'lambda.min')
table(predytrain,trainy)
predyvalidation <- predict(cvfit, newx=validationx,
type="class", s = 'lambda.min')
table(predyvalidation,validationy)
plot(cvfit)
coef(cvfit, s=cvfit$lambda.min)
s=cvfit$lambda.min
```

**Table S3**

| Significant variables are in red | *n* | mean | standard deviation | minimum | maximum | missing% | *IDH*-mut only (*n* = 63) mean (sd) | *IDH*, *TERT* co-mutated (*n* = 66) mean (sd) | *IDH*-wt (*n* = 70) mean (sd) | *p* |
|---|---|---|---|---|---|---|---|---|---|---|
| T2_Mean | 199 | 113.3 | 24.3 | 54.4 | 189.2 | 0 | 121.79 (25.91) | 112.27 (21.60) | 106.67 (23.36) | 0.001 |
| T2_SD | 199 | 21.2 | 7.5 | 8.2 | 44.5 | 0 | 22.68 (7.30) | 22.47 (7.07) | 18.60 (7.38) | 0.001 |
| T2_Max | 199 | 179.2 | 36.9 | 100 | 255 | 0 | 183.98 (34.45) | 186.27 (38.30) | 168.31 (35.71) | 0.008 |
| T2_Min | 199 | 31.5 | 21 | 1 | 84 | 0 | 25.84 (21.27) | 27.02 (19.23) | 40.86 (19.42) | <0.001 |
| T2_Median | 199 | 114 | 25.9 | 46 | 198 | 0 | 123.76 (28.52) | 112.08 (22.12) | 107.07 (24.34) | 0.001 |
| T2_Mode | 199 | 116.7 | 30.7 | 38 | 215 | 0 | 128.54 (33.35) | 113.44 (27.10) | 109.06 (28.58) | 0.001 |
| T2_Entropy | 199 | 6.2 | 0.5 | 4.9 | 7.3 | 0 | 6.32 (0.47) | 6.38 (0.41) | 6.02 (0.53) | <0.001 |
| T2Edge_Mean | 199 | 41 | 17.5 | 14.7 | 98 | 0 | 43.53 (17.67) | 41.62 (14.43) | 38.02 (19.67) | 0.18 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| T2Edge_SD | 199 | 32.2 | 13 | 10 | 70.8 | 0 | 34.93 (13.39) | 34.19 (13.34) | 27.78 (11.38) | 0.002 |
| T2Edge_Max | 199 | 245.1 | 94.9 | 51.6 | 531.2 | 0 | 267.22 (88.49) | 267.41 (97.28) | 204.22 (85.29) | <0.001 |
| T2Edge_Min | 199 | 1.6 | 2.5 | 1 | 25.5 | 0 | 1.24 (0.52) | 1.27 (0.68) | 2.18 (4.12) | 0.046 |
| T2Edge_Median | 199 | 32.8 | 15.8 | 9.5 | 100.4 | 0 | 34.53 (15.65) | 32.63 (12.06) | 31.50 (18.90) | 0.544 |
| T2Edge_Mode | 199 | 12.8 | 8.4 | 1 | 70 | 0 | 12.79 (6.63) | 12.59 (7.46) | 12.88 (10.52) | 0.98 |
| T2Edge_Entropy | 199 | 5.2 | 0.5 | 3.9 | 6.5 | 0 | 5.38 (0.52) | 5.33 (0.48) | 5.03 (0.52) | <0.001 |
| T1_Mean | 191 | 80.6 | 20.4 | 40.9 | 213.3 | 4 | 77.89 (19.36) | 78.85 (18.45) | 84.62 (22.49) | 0.125 |
| T1_SD | 191 | 14 | 5.3 | 5 | 47.7 | 4 | 15.14 (6.13) | 14.40 (5.45) | 12.64 (3.85) | 0.021 |
| T1_Max | 191 | 141 | 43.6 | 70 | 255 | 4 | 148.69 (47.59) | 140.33 (41.33) | 134.70 (41.31) | 0.191 |
| T1_Min | 191 | 16.8 | 18 | 1 | 97 | 4 | 12.18 (12.75) | 13.48 (15.28) | 24.22 (21.92) | <0.001 |
| T1_Median | 191 | 80.9 | 20.5 | 38 | 216 | 4 | 77.61 (19.42) | 79.21 (18.56) | 85.40 (22.64) | 0.073 |
| T1_Mode | 191 | 80.3 | 21.8 | 17 | 219 | 4 | 76.67 (20.62) | 78.62 (18.92) | 85.04 (24.69) | 0.073 |

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|---|---|---|---|---|---|---|---|---|---|---|
| T1_Entropy | 191 | 5.6 | 0.4 | 4.2 | 7.5 | 4 | 5.75 (0.41) | 5.68 (0.45) | 5.44 (0.38) | <0.001 |
| T1Gd_Mean | 189 | 84 | 22.9 | 15.2 | 164.7 | 5 | 80.08 (23.78) | 81.35 (18.06) | 90.25 (25.15) | 0.022 |
| T1Gd_SD | 189 | 16 | 8 | 3.3 | 44.8 | 5 | 16.17 (7.52) | 14.75 (7.41) | 16.89 (8.80) | 0.305 |
| T1Gd_Max | 189 | 173.7 | 51.6 | 39 | 255 | 5 | 180.36 (49.93) | 162.94 (46.94) | 177.58 (56.36) | 0.13 |
| T1Gd_Min | 189 | 24.5 | 18.1 | 1 | 108 | 5 | 21.28 (16.74) | 18.95 (11.68) | 32.70 (21.27) | <0.001 |
| T1Gd_Median | 189 | 82.9 | 22.3 | 15 | 159 | 5 | 79.07 (23.82) | 80.71 (17.28) | 88.59 (24.17) | 0.034 |
| T1Gd_Mode | 189 | 80.3 | 24.2 | 1 | 156 | 5 | 75.21 (25.89) | 78.50 (20.29) | 86.56 (24.94) | 0.023 |
| T1Gd_Entropy | 189 | 5.7 | 0.6 | 3.7 | 7.1 | 5 | 5.73 (0.58) | 5.62 (0.56) | 5.68 (0.67) | 0.63 |
| Gdzscore_Mean | 189 | 0.5 | 0.7 | -0.5 | 3 | 5 | 0.47 (0.67) | 0.48 (0.62) | 0.65 (0.74) | 0.219 |
| Gdzscore_SD | 189 | 0.5 | 0.4 | 0.1 | 2.1 | 5 | 0.49 (0.33) | 0.50 (0.37) | 0.61 (0.40) | 0.135 |
| Gdzscore_Max | 189 | 4.7 | 2.1 | 0.4 | 11 | 5 | 4.91 (1.88) | 4.45 (1.97) | 4.71 (2.36) | 0.486 |
| Gdzscore_Min | 189 | -1.2 | 1.4 | -12.3 | 1.2 | 5 | -1.33 (1.42) | -1.39 (1.79) | -0.94 (0.96) | 0.162 |
| Gdzscore_Median | 189 | 0.4 | 0.7 | -0.5 | 2.6 | 5 | 0.41 (0.67) | 0.40 (0.57) | 0.51 (0.71) | 0.589 |
| Gdzscore_Mode | 189 | 0 | 1.2 | -9.7 | 2.5 | 5 | -0.04 (0.94) | -0.15 (1.49) | 0.11 (0.97) | 0.443 |

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|---|---|---|---|---|---|---|---|---|---|---|
| Gdzscore_Entropy | 189 | 4 | 0.7 | 2.7 | 6.2 | 5 | 3.93 (0.60) | 3.89 (0.66) | 4.16 (0.81) | 0.059 |
| FLAIR_Mean | 178 | 126.8 | 31.4 | 54.7 | 213.8 | 10.6 | 124.94 (31.23) | 130.98 (30.51) | 124.55 (32.52) | 0.461 |
| FLAIR_SD | 178 | 28.3 | 10.5 | 9.8 | 62.4 | 10.6 | 27.75 (9.77) | 31.37 (10.84) | 25.94 (10.15) | 0.015 |
| FLAIR_Max | 178 | 191.2 | 42.7 | 88 | 255 | 10.6 | 188.03 (42.10) | 201.19 (40.87) | 184.64 (44.00) | 0.082 |
| FLAIR_Min | 178 | 10.4 | 19 | 1 | 118 | 10.6 | 8.07 (19.15) | 7.61 (12.21) | 15.33 (23.00) | 0.042 |
| FLAIR_Median | 178 | 130.7 | 33.1 | 56 | 229 | 10.6 | 128.46 (32.63) | 135.86 (32.50) | 127.85 (33.99) | 0.342 |
| FLAIR_Mode | 178 | 142.2 | 48.9 | 50 | 255 | 10.6 | 138.16 (46.11) | 148.32 (48.69) | 140.08 (51.73) | 0.49 |
| FLAIR_Entropy | 178 | 6.5 | 0.5 | 5.1 | 7.5 | 10.6 | 6.52 (0.49) | 6.69 (0.44) | 6.37 (0.48) | 0.001 |
| Gdzscore_area_of_Gd | 189 | 0 | 0 | 0 | 0 | 5 | 0.00 (0.01) | 0.00 (0.01) | 0.00 (0.01) | 0.974 |
| MNI_str_loc.01 | 199 | 0.1 | 0.1 | 0 | 0.6 | 0 | 0.12 (0.06) | 0.11 (0.06) | 0.17 (0.13) | <0.001 |
| MNI_str_loc.02 | 199 | 0 | 0.1 | 0 | 0.3 | 0 | 0.03 (0.05) | 0.03 (0.03) | 0.04 (0.07) | 0.22 |
| MNI_str_loc.03 | 199 | 0 | 0.1 | 0 | 1 | 0 | 0.02 (0.12) | 0.00 (0.00) | 0.04 (0.17) | 0.222 |
| MNI_str_loc.04 | 199 | 0.4 | 0.3 | 0 | 1 | 0 | 0.42 (0.35) | 0.55 (0.34) | 0.25 (0.29) | <0.001 |
| MNI_str_loc.05 | 199 | 0 | 0.1 | 0 | 0.5 | 0 | 0.05 (0.08) | 0.04 (0.07) | 0.05 (0.08) | 0.811 |

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|---|---|---|---|---|---|---|---|---|---|---|
| MNI_str_loc.06 | 199 | 0 | 0.1 | 0 | 0.5 | 0 | 0.02 (0.07) | 0.01 (0.04) | 0.02 (0.06) | 0.291 |
| MNI_str_loc.07 | 199 | 0.1 | 0.2 | 0 | 1 | 0 | 0.11 (0.18) | 0.12 (0.24) | 0.12 (0.19) | 0.887 |
| MNI_str_loc.08 | 199 | 0 | 0.1 | 0 | 0.9 | 0 | 0.03 (0.04) | 0.02 (0.04) | 0.05 (0.12) | 0.19 |
| MNI_str_loc.09 | 199 | 0.2 | 0.3 | 0 | 1 | 0 | 0.18 (0.26) | 0.11 (0.24) | 0.19 (0.28) | 0.161 |
| MNI_str_loc.10 | 199 | 0 | 0.1 | 0 | 0.8 | 0 | 0.02 (0.03) | 0.01 (0.02) | 0.07 (0.17) | 0.001 |
| HrvdOxf_loc.01 | 199 | 21.4 | 20.2 | 0 | 100 | 0 | 18.39 (14.09) | 13.99 (9.10) | 31.10 (27.53) | <0.001 |
| HrvdOxf_loc.02 | 199 | 8.6 | 15.5 | 0 | 87.9 | 0 | 7.26 (12.83) | 13.52 (18.93) | 5.30 (13.06) | 0.005 |
| HrvdOxf_loc.03 | 199 | 4.5 | 6.5 | 0 | 37.4 | 0 | 4.41 (5.97) | 3.94 (5.97) | 5.03 (7.49) | 0.621 |
| HrvdOxf_loc.04 | 199 | 7.4 | 13 | 0 | 63.1 | 0 | 8.81 (14.14) | 10.05 (15.10) | 3.59 (8.00) | 0.008 |
| HrvdOxf_loc.05 | 199 | 6.1 | 10.7 | 0 | 87.4 | 0 | 7.52 (14.69) | 8.07 (9.95) | 3.06 (5.16) | 0.01 |
| HrvdOxf_loc.06 | 199 | 1.4 | 2.6 | 0 | 21.2 | 0 | 1.53 (2.85) | 1.88 (3.26) | 0.87 (1.21) | 0.068 |
| HrvdOxf_loc.07 | 199 | 1.5 | 2.2 | 0 | 14.8 | 0 | 1.72 (2.57) | 1.56 (1.87) | 1.25 (2.00) | 0.436 |
| HrvdOxf_loc.08 | 199 | 6.4 | 11.2 | 0 | 70.5 | 0 | 6.38 (12.42) | 6.80 (12.22) | 6.01 (8.92) | 0.918 |
| HrvdOxf_loc.09 | 199 | 1.9 | 3.4 | 0 | 21.7 | 0 | 2.32 (3.97) | 1.53 (3.06) | 1.78 (3.21) | 0.411 |
| HrvdOxf_loc.10 | 199 | 0.8 | 1.3 | 0 | 9.1 | 0 | 0.65 (0.71) | 0.75 (1.35) | 0.87 (1.64) | 0.635 |
| HrvdOxf_loc.11 | 199 | 1.1 | 2.2 | 0 | 18.1 | 0 | 1.09 (1.89) | 0.99 (2.68) | 1.13 (2.05) | 0.928 |

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|---|---|---|---|---|---|---|---|---|---|---|
| HrvdOxf_loc.12 | 199 | 0.8 | 1.4 | 0 | 9.6 | 0 | 0.79 (1.11) | 0.67 (1.47) | 0.80 (1.48) | 0.816 |
| HrvdOxf_loc.13 | 199 | 1.9 | 5.1 | 0 | 43.2 | 0 | 2.07 (4.02) | 1.76 (6.24) | 1.90 (4.97) | 0.942 |
| HrvdOxf_loc.14 | 199 | 0.8 | 1.9 | 0 | 14.7 | 0 | 1.27 (2.59) | 0.48 (1.45) | 0.71 (1.28) | 0.048 |
| HrvdOxf_loc.15 | 199 | 0.5 | 0.7 | 0 | 4.5 | 0 | 0.61 (0.84) | 0.37 (0.55) | 0.45 (0.60) | 0.119 |
| HrvdOxf_loc.16 | 199 | 1 | 2.1 | 0 | 12.9 | 0 | 1.34 (2.47) | 0.64 (1.86) | 0.89 (1.89) | 0.16 |
| HrvdOxf_loc.17 | 199 | 0.5 | 0.9 | 0 | 7.1 | 0 | 0.70 (1.22) | 0.31 (0.62) | 0.47 (0.90) | 0.065 |
| HrvdOxf_loc.18 | 199 | 3.1 | 7.6 | 0 | 65.3 | 0 | 1.93 (4.20) | 3.85 (8.61) | 3.53 (8.85) | 0.309 |
| HrvdOxf_loc.19 | 199 | 1.2 | 3.2 | 0 | 23 | 0 | 1.00 (2.42) | 1.17 (3.64) | 1.30 (3.38) | 0.871 |
| HrvdOxf_loc.20 | 199 | 0.9 | 2.8 | 0 | 28.2 | 0 | 0.48 (0.79) | 1.40 (4.53) | 0.78 (1.61) | 0.165 |
| HrvdOxf_loc.21 | 199 | 1 | 2.2 | 0 | 17.3 | 0 | 0.93 (1.55) | 0.97 (2.63) | 1.01 (2.35) | 0.977 |
| HrvdOxf_loc.22 | 199 | 0.9 | 3.1 | 0 | 31.8 | 0 | 1.13 (3.24) | 0.63 (1.93) | 0.93 (3.82) | 0.657 |
| HrvdOxf_loc.23 | 199 | 1.7 | 7.8 | 0 | 75.1 | 0 | 2.05 (8.14) | 2.12 (10.67) | 0.96 (2.68) | 0.626 |
| HrvdOxf_loc.24 | 199 | 0.3 | 0.6 | 0 | 3.9 | 0 | 0.41 (0.70) | 0.16 (0.12) | 0.42 (0.75) | 0.019 |
| HrvdOxf_loc.25 | 199 | 0.3 | 0.4 | 0 | 3.7 | 0 | 0.28 (0.34) | 0.21 (0.24) | 0.27 (0.46) | 0.495 |
| HrvdOxf_loc.26 | 199 | 0.7 | 1.7 | 0 | 14.5 | 0 | 0.56 (1.03) | 1.00 (2.58) | 0.48 (1.01) | 0.167 |
| HrvdOxf_loc.27 | 199 | 1.6 | 3.4 | 0 | 24.1 | 0 | 1.58 (2.98) | 2.04 (3.90) | 1.34 (3.31) | 0.476 |
| HrvdOxf_loc.28 | 199 | 1.2 | 3.2 | 0 | 25.4 | 0 | 1.29 (3.24) | 1.49 (4.16) | 0.93 (2.00) | 0.594 |

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|---|---|---|---|---|---|---|---|---|---|---|
| HrvdOxf_loc.29 | 199 | 3.3 | 6 | 0 | 40.5 | 0 | 3.84 (7.41) | 4.52 (6.22) | 1.71 (3.85) | 0.018 |
| HrvdOxf_loc.30 | 199 | 3.6 | 7.9 | 0 | 65.1 | 0 | 3.06 (4.85) | 3.89 (6.97) | 3.82 (10.55) | 0.805 |
| HrvdOxf_loc.31 | 199 | 1.5 | 3.9 | 0 | 24.5 | 0 | 1.73 (4.18) | 0.40 (1.33) | 2.43 (4.82) | 0.008 |
| HrvdOxf_loc.32 | 199 | 1 | 2.8 | 0 | 19 | 0 | 1.53 (3.58) | 0.44 (1.78) | 1.11 (2.75) | 0.083 |
| HrvdOxf_loc.33 | 199 | 0.2 | 0.3 | 0 | 2.4 | 0 | 0.22 (0.36) | 0.15 (0.20) | 0.22 (0.24) | 0.221 |
| HrvdOxf_loc.34 | 199 | 1.6 | 3.4 | 0 | 30.8 | 0 | 1.61 (2.58) | 1.52 (3.14) | 1.66 (4.18) | 0.97 |
| HrvdOxf_loc.35 | 199 | 0.9 | 2.1 | 0 | 18.9 | 0 | 1.05 (1.69) | 0.44 (0.98) | 1.20 (3.04) | 0.089 |
| HrvdOxf_loc.36 | 199 | 0.5 | 1.4 | 0 | 10.2 | 0 | 0.58 (1.17) | 0.18 (0.46) | 0.86 (1.98) | 0.016 |
| HrvdOxf_loc.37 | 199 | 0.5 | 2.1 | 0 | 22.5 | 0 | 0.66 (1.76) | 0.10 (0.19) | 0.84 (3.07) | 0.1 |
| HrvdOxf_loc.38 | 199 | 0.3 | 0.7 | 0 | 6.5 | 0 | 0.41 (0.66) | 0.22 (0.49) | 0.39 (0.96) | 0.264 |
| HrvdOxf_loc.39 | 199 | 0.6 | 1.4 | 0 | 10.5 | 0 | 0.83 (1.23) | 0.30 (0.74) | 0.79 (1.90) | 0.05 |
| HrvdOxf_loc.40 | 199 | 0.3 | 0.6 | 0 | 6.6 | 0 | 0.37 (0.59) | 0.12 (0.18) | 0.30 (0.91) | 0.079 |
| HrvdOxf_loc.41 | 199 | 0.2 | 1.2 | 0 | 16.2 | 0 | 0.14 (0.20) | 0.10 (0.13) | 0.37 (1.93) | 0.348 |
| HrvdOxf_loc.42 | 199 | 0.8 | 1.9 | 0 | 22.6 | 0 | 1.06 (2.90) | 0.85 (1.30) | 0.64 (1.07) | 0.45 |
| HrvdOxf_loc.43 | 199 | 1.8 | 3 | 0 | 18.7 | 0 | 1.63 (2.79) | 1.82 (3.02) | 1.94 (3.07) | 0.833 |
| HrvdOxf_loc.44 | 199 | 0.7 | 1.4 | 0 | 9.7 | 0 | 0.63 (0.99) | 0.60 (1.45) | 0.99 (1.54) | 0.178 |
| HrvdOxf_loc.45 | 199 | 1.1 | 3.4 | 0 | 43.9 | 0 | 0.81 (1.07) | 0.74 (1.48) | 1.84 (5.49) | 0.114 |

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|---|---|---|---|---|---|---|---|---|---|---|
| HrvdOxf_loc.46 | 199 | 0.7 | 1.6 | 0 | 14.3 | 0 | 0.62 (0.89) | 0.60 (1.20) | 0.96 (2.30) | 0.342 |
| HrvdOxf_loc.47 | 199 | 0.7 | 1.4 | 0 | 8 | 0 | 0.71 (1.40) | 0.60 (1.51) | 0.76 (1.45) | 0.815 |
| HrvdOxf_loc.48 | 199 | 0 | 0.1 | 0 | 0.9 | 0 | 0.02 (0.07) | 0.00 (0.01) | 0.02 (0.12) | 0.2 |
| HrvdOxf_loc.49 | 199 | 0 | 0 | 0 | 0.1 | 0 | 0.00 (0.01) | 0.00 (0.00) | 0.00 (0.00) | 0.342 |
| totalsurfarea | 199 | 15050.6 | 11192.4 | 491 | 49999 | 0 | 17636.05 (12180.26) | 14471.79 (10192.69) | 13269.36 (10892.84) | 0.07 |
| totalvol | 199 | 94275.2 | 90619.7 | 692 | 401665 | 0 | 116158.73 (97729.66) | 94462.20 (90880.79) | 74403.57 (79775.64) | 0.029 |
| compactness01 | 199 | 73.9 | 38.8 | 6.3 | 168.6 | 0 | 84.77 (38.38) | 77.32 (38.09) | 60.89 (36.62) | 0.001 |
| compactness02 | 199 | 0 | 0 | 0 | 0.1 | 0 | 0.00 (0.00) | 0.00 (0.00) | 0.00 (0.01) | 0.017 |
| spherical_disproportion | 199 | 1.6 | 0.2 | 1.2 | 2.3 | 0 | 1.57 (0.21) | 1.53 (0.13) | 1.64 (0.25) | 0.009 |
| sphericity | 199 | 2 | 0.2 | 1.3 | 2.5 | 0 | 2.03 (0.24) | 2.07 (0.16) | 1.96 (0.28) | 0.031 |
| surface_volume_ratio | 199 | 0.2 | 0.1 | 0.1 | 0.7 | 0 | 0.19 (0.06) | 0.19 (0.05) | 0.26 (0.12) | <0.001 |

**Fig. S1. Location mapping on MNI152 in the axial plane.** Color-coded voxel-wise lesion mapping of the three different molecular subtypes of this cohort. Frequency of the locations of the brain affected by each molecular subtype are color coded as indicated.

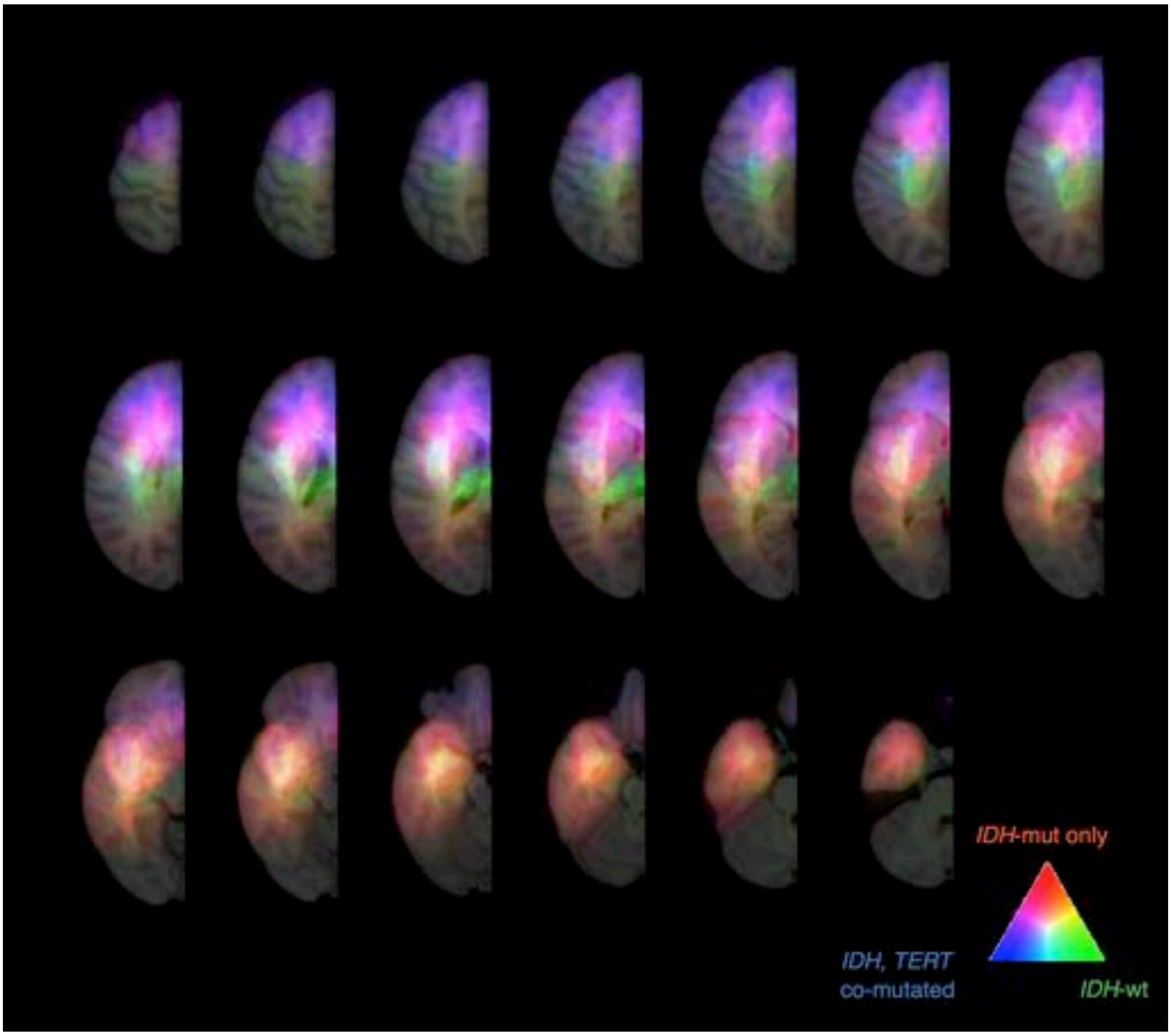

**Fig. S2. Location mapping on MNI152 in the coronal plane.** Color-coded voxel-wise lesion mapping of the three different molecular subtypes of this cohort. Frequency of the locations of the brain affected by each molecular subtype are color coded as indicated.

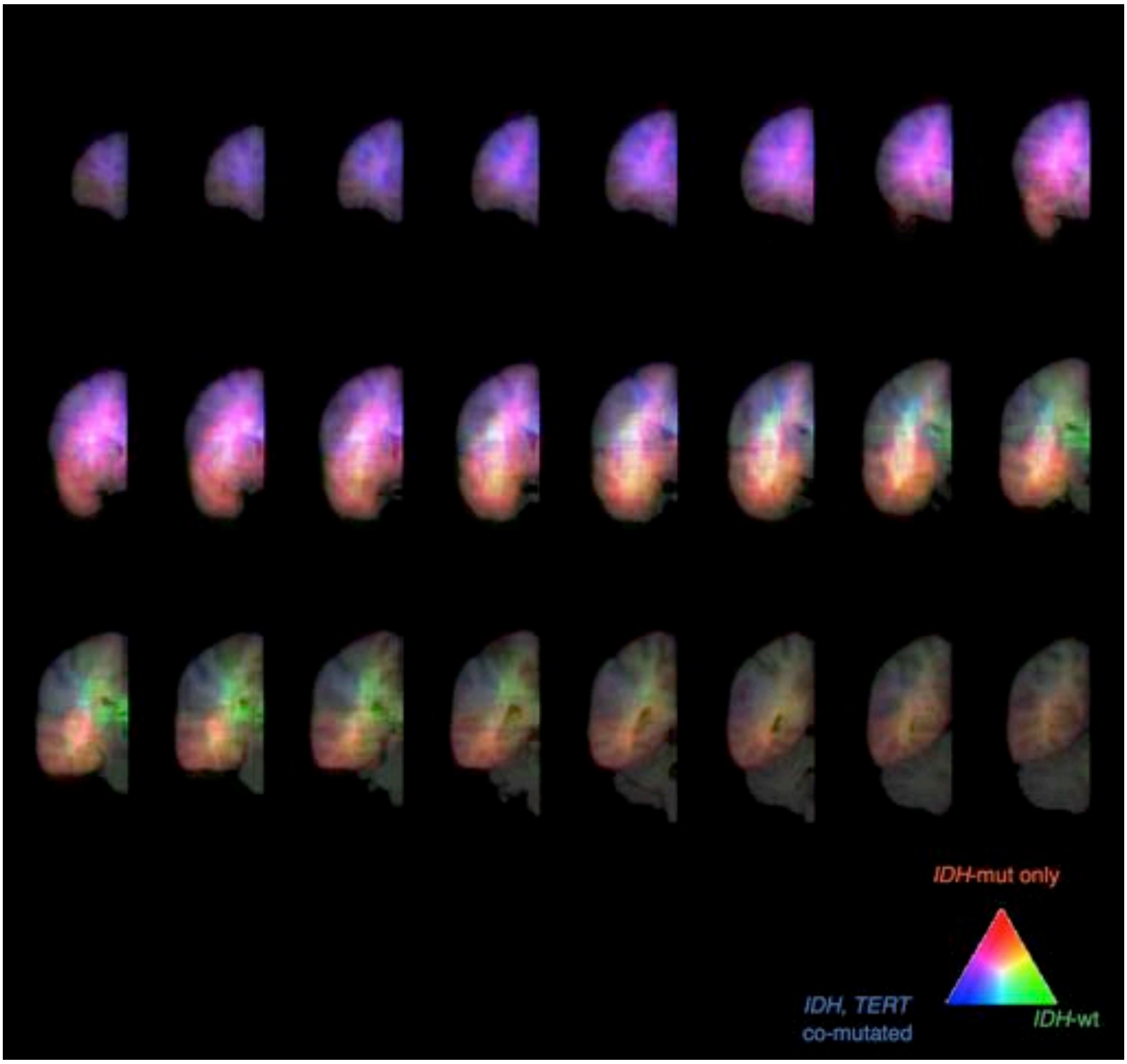

**Fig. S3. Location mapping on MNI152 in the sagittal plane.** Color-coded voxel-wise lesion mapping of the three different molecular subtypes of this cohort. Frequency of the locations of the brain affected by each molecular subtype are color coded as indicated.

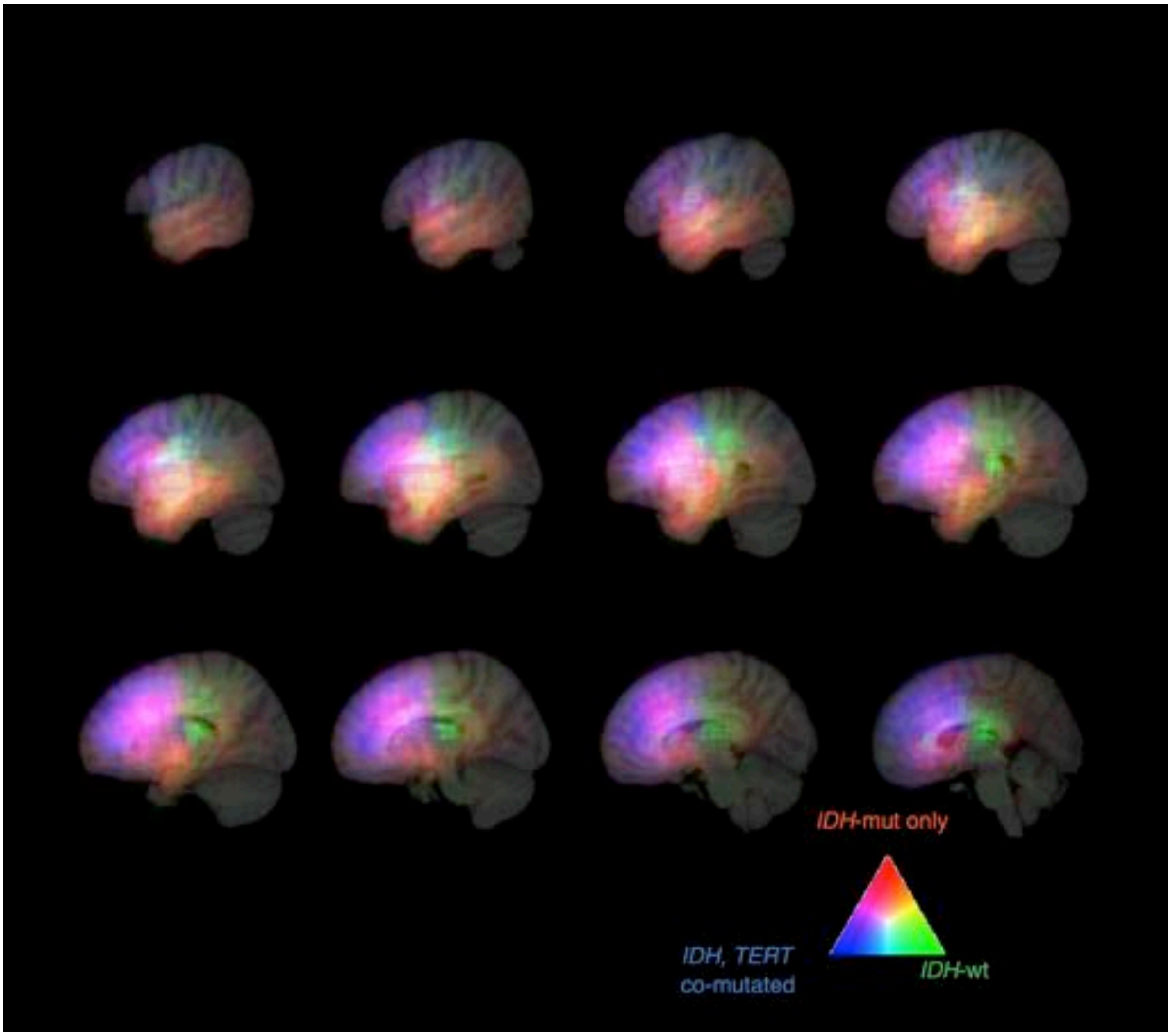

**Fig. S4. Random permutation analysis mapping in the axial plane.** Random permutation analysis shows locations that exhibited statistically significant differences in spatial distribution of the lesion among the three different molecular subtypes of the analyzed cohort.