**Supplementary Material**

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**VI. Fractal-based features** [2]

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2. Median fractal dimension
3. Minimal fractal dimension
4. Maximal fractal dimension
5. Fractal dimension standard deviation

**B. The Selected Features for Radiomics Signature of Each Outcome and Their Definitions**

**1.Total Recurrence**

* ***F\_morph.pca.flatness.peritumor*** = Flatness – Morphological feature (3.1.16)

The ratio of the major and least axis lengths could be viewed as the extent to which a volume is flat relative to its length. For computational reasons, we express flatness as an inverse ratio. “1” is thus completely non-flat, e.g., a sphere, and smaller values express objects which are increasingly flatter.



* ***F\_cm.inv.var.peritumor*** = Inverse variance – Textural gray level co-occurrence feature (3.6.18)



Where p\_ij is the joint probability of grey levels, i and j occurring in neighboring voxels.

* ***F\_stat.90thpercentile.gtv*** = 90th percentile – statistical feature (3.3.8)

Let Xgl = {Xgl\_1, Xgl\_2,… , Xgl\_Nv} be the set of grey levels of the Nv voxels included in the ROI intensity mask.

F\_stat.90thpercentile is the 90th percentile of Xgl.

* ***F\_szm.glnu.norm.peritumor*** = Grey level non-uniformity normalized – Textural gray level co-occurrence feature (3.8.10)

This is a normalized version of the grey level non-uniformity feature, where the latter assesses the distribution of runs over the grey values. The feature value is low when runs are equally distributed along grey levels. It is defined as:



**2. Local Recurrence**

* ***F\_morph.pca.flatness.gtv*** = Flatness – Morphological feature (3.1.16)



The ratio of the major and least axis lengths could be viewed as the extent to which a volume is flat relative to its length. For computational reasons, we express flatness as an inverse ratio. “1” is thus completely non-flat, e.g., a sphere, and smaller values express objects which are increasingly flatter.

* ***F\_rlm.rl.entr.gtv*** = Run entropy – gray level run length feature (3.7.16)



* ***F\_szm.z.perc.gtv*** = Zone percentage – Textural size zone feature (3.8.13)

This feature assesses the fraction of the number of realised zones and the maximum number of potential zones. Highly uniform ROIs produce a low zone percentage. It is defined as:



* ***F\_morph.av.gtv*** = Surface to volume ratio – Morphological feature (3.1.4)

The surface to volume ratio is given as:



* ***F\_stat.var.gtv*** = Variance – Statistical feature (3.3.2)

Let Xgl = {Xgl\_1, Xgl\_2,… , Xgl\_Nv} be the set of grey levels of the Nv voxels included in the ROI intensity mask. The grey level variance of Xgl is defined as:



**3. Distant metastasis**

* ***F\_cm.inv.var.peritumor*** = Inverse variance – Textural gray level co-occurrence feature (3.6.18)



* ***F\_rlm.srhge.gtv*** = Short run high grey level emphasis – Textural run length feature (3.7.6)

This feature emphasizes runs in the lower left quadrant of the GLRLM, where short run lengths and high grey levels are located. The feature is defined as:



* ***F\_morph.pca.least.gtv*** = Least axis length – Morphological feature (3.1.14)

The least axis is the axis along which the object is least extended. The least axis length is twice the semi-axis length *c*, determined using the smallest eigenvalue obtained by PCA, as described in Section 3.1.12:



* ***F\_rlm.lrhge.gtv*** = Long run high grey level emphasis - Textural run length feature (3.7.8)

This feature emphasizes runs in the lower right quadrant of the GLRLM, where long run lengths and high grey levels are located. The feature is defined as:



* ***F\_rlm.sre.gtv*** = Short runs emphasis - Textural run length feature (3.7.1 )

This feature emphasizes short run lengths. It is defined as:



**D. References**

1. Zwanenburg A, Leger S, Vallières M, Löck S, Initiative for the IBS. Image biomarker standardisation initiative. 2016. Available from: http://arxiv.org/abs/1612.07003. Accessed 5 April 2019

2. Cusumano D, Dinapoli N, Boldrini L, Chiloiro G, Gatta R, Masciocchi C. Fractal‑based radiomic approach to predict complete pathological response after chemo‑radiotherapy in rectal cancer. *Radiol Med*. 2018;123(4):286–95