Supplementary Material —
Formulas for Tumor Texture Analysis

In this supplementary material, the formulas that are used for tumor texture analysis are provided.

1 Unified Notations

The definitions of the textural features make the assumption that the tumor has been delineated as a 3D volume of interest (VOI) in the PET image. We denote $T \subset \mathbb{Z}^3$, the indices of the voxels that are part of the tumor. The value of the SUV signal at the tumor voxel with index $\vec{p} \in T$ is then denoted as $I(\vec{p}) \in \mathbb{R}$.

The most direct way of delineating the tumor volume $T$ consists in thresholding the SUV signal $I$, either with respect to an absolute threshold on the SUV values, or with respect to a relative threshold specified as a percentage of the dynamics of the SUV signal. The segmented volume of interest is then most often tuned manually by the radiation oncologists using specialized 3D contouring software. This kind of semi-automatic delineation is the golden standard that is nowadays used in nuclear medicine departments. Algorithms to automate and improve PET segmentation are still a very active research area that goes beyond the scope of this paper.

With this notation, the SUV intensity features can be readily defined using standard statistics (mean, maximum, minimum, standard deviation, kurtosis, skewness...). As a particular example, the intensity feature corresponding to the mean value of the SUV signal over the tumor is defined as:

$$\sum_{\vec{p} \in T} \frac{I(\vec{p})}{|T|}. \quad (1)$$

2 Gray-Level Co-Occurrence Matrices (GLCM)

Gray-level co-occurrence matrices (GLCM) were originally introduced by Haralick et al. to solve visual classification tasks [1], and have recently been applied to tumor texture analysis, notably by Tixier et al. [2]. In the context of tumor texture analysis, a GLCM matrix encodes the distribution of co-occurring SUV values when a fixed 3D offset is considered.

Let us denote the considered offset as $\vec{\delta} \in \mathbb{Z}^3$. To define the GLCM matrix $C_{\vec{\delta}}$ for the offset $\vec{\delta}$, the dynamics of the SUV values has first to be discretized. Let us define the discretization function $D$ that maps the SUV signal to a set of $n$ discrete values, as follows:

$$D : \mathbb{R} \mapsto \{0, \ldots, n - 1\} : x \mapsto \left\lfloor \frac{n(x - a)}{b - a} \right\rfloor, \text{ with } a = \min_{\vec{p} \in T} I(\vec{p}) \text{ and } b = \max_{\vec{p} \in T} I(\vec{p}). \quad (2)$$
In practice, \( n \) is set to 64. The GLCM matrix \( C_{\vec{\delta}} \in \mathbb{R}^{n \times n} \) is then defined as:

\[
C_{\vec{\delta}}(i,j) = \sum_{\vec{p} \in T} \begin{cases} 1 & \text{if } D(I(\vec{p})) = i \text{ and } D(I(\vec{p} + \vec{\delta})) = j, \\ 0 & \text{otherwise}, \end{cases}
\]

(3)

where \( i, j \in \{0, \ldots, n - 1\} \). Once \( C_{\vec{\delta}} \) is computed for a fixed offset \( \vec{\delta} \), several statistics can be extracted from the GLCM to capture textural features. For instance, the uniformity (aka. angular second-moment) for offset \( \vec{\delta} \) is defined as:

\[
\text{ASM}_{\vec{\delta}} = \sum_{i=0}^{n-1} \sum_{j=0}^{n-1} C_{\vec{\delta}}(i,j)^2.
\]

(4)

Other textural features such as contrast (aka. inertia), entropy, correlation, homogeneity or dissimilarity have been defined in the framework of GLCM [1, 2]. All these textural features are parametrized by the offset \( \vec{\delta} \) of the GLCM. To obtain a single, global value for some textural feature over the tumor volume, it is required to average the value of the feature over a set of \( m \) offsets \( \Delta = \{\vec{\delta}_1, \ldots, \vec{\delta}_m\} \). In practice, Tixier et al. define \( \Delta \) as the set of offsets to neighbors in 3D space with 26-connexity [3, page 92]:

\[
\Delta = \{-1, 0, 1\}^3 \setminus \{(0, 0, 0)\}.
\]

(5)

Going back to the particular example of uniformity (cf. Equation 4), the global GLCM uniformity over the tumor volume is finally be defined as:

\[
\sum_{\vec{\delta} \in \Delta} \frac{\text{ASM}_{\vec{\delta}}}{|\Delta|}.
\]

(6)

3 Neighborhood Gray-Tone Difference Matrix

The second class of textural features that is implemented in our open framework is built on the top of the neighborhood gray-tone difference matrices (NGTDM), originally proposed by Amadasum and King [4]. NGTDM were applied to tumor texture analysis by Yu et al. [5]. In this context, a NGTDM matrix \( S \) is a column vector that sums up the differences between the discretized SUV value of a voxel and the discretized, average SUV value of the neighbors of this voxel.

Mathematically, if \( * \) denotes 3-dimensional convolution, \( S \) is defined as:

\[
S_i = \sum_{\vec{p} \in T} \left| D(I(\vec{p})) - D((I * K)(\vec{p})) \right|,
\]

(7)

where \( i \in \{0, \ldots, n - 1\} \) spans the discretized values of the SUV signal, and where \( K \) is the convolution kernel. In practice, this convolution kernel is taken as the averaging 3D filter over the surrounding voxels in 3D space with 26-connexity. Let us also define the \( P \) column vector that, for each discrete SUV level, counts the number of voxels with such a level:

\[
P_i = \left| \{\vec{p} \in T \mid D(I(\vec{p})) = i\} \right|.
\]

(8)
and $g$ as the number of discrete levels for which at least one voxel maps to this level:

$$g = \left| \{ i = 0, \ldots, n - 1 \mid P_i > 0 \} \right|. \quad (9)$$

Given $S$, $P$ and $g$, several textural features can now be defined [4]:

**coarseness**

$$\text{coarseness} = 1 \left( \epsilon + \sum_{i=0}^{n-1} P_i S_i \right), \quad (10)$$

**contrast**

$$\text{contrast} = \frac{1}{g(g-1)} \left( \sum_{i=0}^{n-1} \sum_{j=0}^{n-1} P_i P_j (i-j)^2 \right) \left( \sum_{i=0}^{n-1} S_i \right) \left( \sum_{i=0}^{n-1} P_i \right), \quad (11)$$

**busyness**

$$\text{busyness} = \left( \sum_{i=0}^{n-1} P_i S_i \right) \left( \sum_{i=0}^{n-1} \sum_{j=0}^{n-1} |iP_i - jP_j| \right) \text{ with } P_i \neq 0, P_j \neq 0, \quad (12)$$

where $\epsilon$ is a small constant to ensure numerical stability. As summarized by Yu et al., “coarseness refers to the density of the edge element (the finer the texture, the higher the edge density), contrast is related to the dynamic range of gray-levels in an image, and busyness is a measure of spatial rate of gray-level change” [5].

### 4 Intensity and Size-Zone Variability of Connected Components

The previously introduced features were either global (volume and intensity features describe the tumor as a whole), or local (GLCM and NGTDM capture the neighborhood of the voxels). This contrasts with a third category of textural features that describe the relative properties of sub-regions of the full tumor volume [6, 3]. These sub-regions are defined as the connected components of the tumor volume whose voxels share the same SUV level after discretization.

Mathematically, we first construct an undirected graph $G = (T, E)$ whose vertices $T$ correspond to the indices of the voxels in the tumor volume, and whose edges $E \subseteq T \times T$ link neighboring voxels with the same discrete level:

$$(\vec{p}, \vec{q}) \in E \text{ iff } D(I(\vec{p})) = D(I(\vec{q})) \text{ and } \vec{q} \in \mathcal{N}(\vec{p}), \quad (13)$$

where $\mathcal{N}(\vec{p})$ designates the set of neighbors of the voxel with index $\vec{p} \in T$. In practice, $\mathcal{N}$ is taken as the 6-connexity in 3D space. The $m$ connected components $\{C_1, \ldots, C_m\}$ of the graph $G$ can then be extracted through the well-known union-find algorithm [7]. Each connected component $C_i \subseteq T$ of index $i = 1, \ldots, m$ corresponds to a 3D sub-region of the tumor volume, of which all the voxels share the same discrete SUV level denoted $L_i \in \{0, \ldots, n - 1\}$.

Once the set of connected components is known, new textural features can be introduced by considering the matrix $A$ can collects, for each discrete level $l \in \{0, \ldots, n - 1\}$, the distribution of the sizes $s$ of the connected components corresponding to this level:

$$A(l, s) = \left| \{ C_i \mid L_i = l \text{ and } |C_i| = s \} \right|. \quad (14)$$
The matrix $A$ has $n$ rows (one for each discrete SUV level), and $|T| + 1$ columns (one for each possible size of a connected component). The intensity variability (IV) and the size-zone variability (SZV) are then derived from $A$ as follows [3, Table 4.2]:

$$\text{IV} = \frac{1}{m} \sum_{l=0}^{n-1} \left( \sum_{s=0}^{|T|} A(l, s) \right)^2$$ \hspace{1cm} (15)

$$\text{SZV} = \frac{1}{m} \sum_{s=0}^{|T|} \left( \sum_{l=0}^{n-1} A(l, s) \right)^2$$ \hspace{1cm} (16)

The intensity variability describes the distribution of the intensity of the connected components, whereas size-zone variability captures the distribution of their sizes.

References


