SEMI-AUTOMATIC COMPUTATION METHOD FOR BPI_{VOL} AND BPI_{SUV}

After loading the PET and CT images, following steps were used for the computation of BPI_{VOL} and BPI_{SUV}:

Bed Removal in CT

The CT image was first thresholded at 15% of the range of its intensities (for an image with intensities between -1024 and 2500 Hounsfield Units, the threshold is -495.4 Hounsfield Units). From the resulting mask, the size of all connected components were computed. The biggest connected component was kept as the body mask. A further step of morphological hole closing was applied to each slice of the body mask to fill in the lungs and potential air in the abdomen. The bed, being outside of the body mask, was masked out of the image.

Bone Segmentation in CT

For the segmentation of the skeleton from CT, we used the first two steps of the method of Kang et al. *(10)*.

Global thresholding. First, a low and a high threshold were computed by fitting a mixture of two Gaussian distributions $G_1(m_1,\sigma_1)$ and $G_2(m_2,\sigma_2)$ with respective means m_1 and m_2 and respective standard deviations σ_1 and σ_2 to the histogram of CT intensities (excluding the background). Without loss of generality, we assumed $m_1<m_2$. After fitting, the low threshold LT was computed as:

$$LT = \min(160,\ m_2+1.7\ \sigma_2)$$

The high threshold HT was computed as:

$$HT = LT+400$$

All pixels that had an intensity superior to HT were considered as bone. All pixels that had an intensity inferior to LT were considered as not bone. All pixels that had an intensity between LT

and HT were considered as undetermined and were labelled in the next step. To avoid labelling endoprothesis as bones, all pixels with an intensity above 2000 were excluded from the bone mask.

Local thresholding. In a second step, the pixels that could not be labelled by global thresholding were considered. For each pixel, the local mean m_{loc} and local standard deviation SD_{loc} were computed within a 26-pixels neighbourhood. If the intensity of the pixel was superior to m_{loc} – 0.8 SD_{loc}, it was labelled as bone, otherwise as not bone.

Morphological operations. To further correct the segmentation and include the bone marrow, morphological operations were applied. All connected components with a size inferior to 45 pixels were removed. The bone mask was dilated by one pixel, hole filling was applied to each slice and the bone mask was eroded by one pixel.

Lesions segmentation in PET

^{68}Ga-PSMA usually does not exhibit unspecific uptake in the bones and bone marrow. Therefore, regions of the skeleton with increased uptake can be considered as bone metastases. First, the SUV image was computed using the patient weight, injection time and acquisition time contained in the image header. Since the PET and the CT had been acquired in the same session on the same scanner, they were intrinsically aligned. The bone mask computed from the CT image was therefore applied to the SUV image to determine the location of bones. A user-chosen threshold was further applied to the bone locations to compute abnormal uptake. Normal uptake sites such as the kidneys are automatically excluded from the computation because they are not part of the bone mask.

BPI$_{VOL}$ and BPI$_{SUV}$ computation

After having computed the bone and the lesion masks, BPI$_{VOL}$ and BPI$_{SUV}$ were computed using their respective definitions, where N is the number of pixels p that belong to bone metastases:

$$BPI_{VOL} = 100 \times \frac{Bone\ metastases\ volume}{Skeleton\ volume} \qquad \text{(no unit)}$$

$$SUV_{mean} = \frac{1}{N} \sum_{\substack{p\ in\ bone \\ metastases}} SUV(p) \qquad \text{(unit: g/mL)}$$

$$BPI_{SUV} = BPI_{VOL} \times SUV_{mean}/100 \qquad \text{(unit: g/mL)}$$

SUV threshold choice

The SUV-threshold for lesion segmentation was chosen by the user. Rather than choosing it arbitrarily, we proposed a method to calculate it using a negative training patients cohort. For the cancer-negative patients, the value of BPI$_{VOL}$ was the percentage of the skeleton that is falsely segmented as lesions.

Since the training cohort was chosen to be negative for cancer, BPI$_{VOL}$ should have been 0 for these patients. However, because of the noise present in PET, in some pixels, the uptake was higher than normal background uptake. Depending on the chosen SUV-threshold, the thresholding of the PET image resulted in a non-empty set of bone lesions and BPI$_{VOL}$ was computed as greater than 0.

We proposed that the user chose a percentage of false positives FP$_{max}$ that he tolerated. For each patient of the cohort, BPI$_{VOL}$ was computed using the method described above with thresholds ranging from 0 to 4 with steps of 0.05. A different BPI$_{VOL}$ value was obtained for each SUV-threshold: with a SUV- threshold of 0, BPI$_{VOL}$ was 100, and with a SUV-threshold of 4, for cancer-negative patients, it was very close to 0. The recommended threshold t$_{rec}$ for the patient was calculated as :

$$t_{rec} = \min\{t \in [0,4] \mid BPI_{VOL} \leq FP_{max}\}$$

The SUV-threshold for the testing cohort was then chosen as the maximum of all t_{rec} obtained for

the training cohort.