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Automated ^{68}Ga -PSMA-PET Total Metabolic Tumor Volume (TMTV) Extraction for Predicting PSA Change in ^{177}Lu -PSMA Therapy

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Introduction

Prostate cancer is a major health concern worldwide, and the treatment of advanced prostate cancer is still challenging. Radiopharmaceutical therapy with ¹⁷⁷Lu-PSMA has emerged as a promising approach to address this issue. PET/CT imaging is commonly used to determine patient eligibility for this treatment, extent of disease and the correlation between PET/CT imaging features and serum PSA levels has been shown to predict treatment outcomes [1]. In this work, we analyzed some correlations between imaging features and PSA levels to highlight the importance of PET/CT imaging in predicting the response to ¹⁷⁷Lu-PSMA therapy. The objective of this study is to predict treatment outcomes with the goal of refining patient eligibility.

Materials & Methods

Patient Data and Imaging:

- 78 male patients (27 responders) who received ¹⁷⁷Lu-PSMA treatment. 1 to 6 cycles of 7.4 GBq.
- ⁶⁸Ga-PSMA PET/CT imaging (at least one).
- SPECT imaging at 24 hours after each treatment cycle.

Image Pre-processing:

- Automatic segmentation method "TotalSegmentator" [2].
- Created two sets of physiological organ masks, expanding one by 5 mm and the other by 10 mm.
 - OAR expanded by 5 mm: gallbladder, stomach, pancreas, small bowel, colon, duodenum, urinary bladder and aorta
 - OAR expanded by 10 mm: liver, kidney right, kidney left and spleen

Lesion Detection (Total Metabolic Tumor Volume):

- Subtracted signal within dilated organ masks from PET image.
- Applied a patient-specific threshold based on mean uptake of all dilated organs at risk (OARs), Figure 1.
- Obtention of the Total Metabolic Tumor Volume: TMTV
- Note: Head region excluded.

Data Analysis:

- First-order statistics on processed treated PET image (mean, max, standard deviation, ...).
- Collected PSA measurements before treatment and after each cycle (1 to 6 cycles).
- Use of PSA Nadir as a target value. PSA Nadir is the minimal PSA value during treatment. A responder is defined as a patient that has a PSA nadir 50% lower than the initial PSA value.
- Calculated Mann-Whitney-U test between the SUV mean of the TMTV and the PSA Nadir as a boolean (responder or not).

Statistical Models:

- Utilized a multilayer perceptron (MLP). Three hidden layers with 100 neurons each.
- Comparison between balanced and unbalanced database.
- Use of a common threshold to all patients (the mean of individual thresholds) of 2.57 SUV.

Comparison with Existing Research:

- Reproduced figure published by Violet et al. [3]

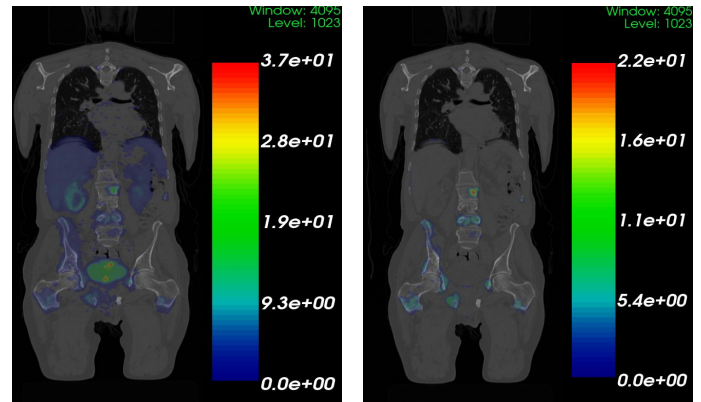


Figure 1. a) The image on the left shows the fusion of the metabolic and anatomical images. b) The image on the right shows our processed image displaying only the tumoral lesions.

Results

Key findings

- The responder and non-responder of the database show a statistical difference when looking for the mean SUV of the TMTV, the p-value is 0.001. The result is the same for the MTV located on the bones (p-value = 0.001), Figure 2.
- The MLP classifier using a balanced database (27 responders and 27 non-responders) has a F1-score of 0.71. The F1 score for the unbalanced dataset is 0.48. Figure 3.
- The last ROC curve is computed from a balanced dataset that has a unique threshold for all the patients (2.57 SUV). The F1 score is 0.75. Figure 4.

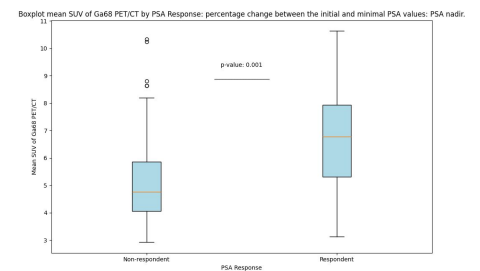


Figure 2. Boxplot depicting the mean SUV of the TMTV from responders and non-responders.

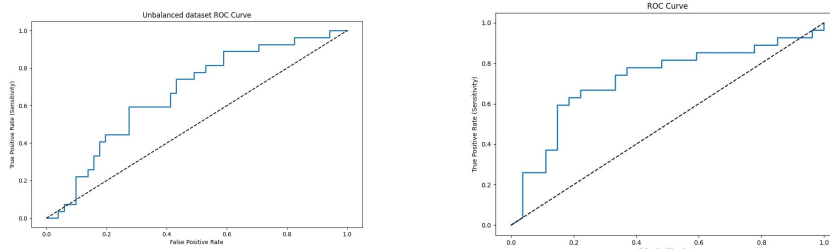


Figure 3. a) Left: ROC curve of the MLP classification performance for the complete (unbalanced) database. b) Right: ROC curve of the balanced database.

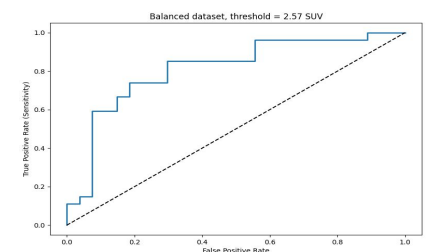


Figure 4. ROC curve of the balanced database for a TMTV computed with an unique threshold.

Conclusion

There is a correlation between the mean SUV of the TMTV and the PSA values. This correlation is weak enough for the classifier to perform poorly on separating responders and non-responders. A larger database ought to be used and/or a newer curated version of the TMTV employed.

References

References: [1] Moazemi et al., May 2021, Annals of Translational Medicine; [2] Wasserthal et al., 2022, arXiv; [3] Violet et al., 2019, JNM