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EDITORIAL

Recent Updates on Applications of Artificial Intelligence for Nuclear Medicine Professionals: Prostate Cancer and PET/CT

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Prostate cancer is one of the most common and life-threatening male cancers worldwide. Early and accurate diagnosis, followed by targeted treatment, is crucial to improving patient survival and quality of life. While traditional diagnostic and treatment methodologies are effective to a certain extent, they often face challenges in terms of consistency, objectivity, and efficiency.

Nuclear medicine, with its innovative tracers such as prostate membrane specific antigen (PSMA), is addressing key challenges in the diagnosis and treatment of prostate cancer. In line with these advances, the field of artificial intelligence (AI) is making significant strides in enhancing PET/CT imaging for prostate cancer, as well as for other areas of nuclear medicine [1, 2]. The synergy of AI with medical imaging is transforming the detection, assessment, and management of prostate cancer, enhancing precision and spurring research into AI-based imaging biomarkers. This minireview examines three pioneering studies that signify a new AI era in the diagnosis and treatment of prostate cancer, illuminating the path towards more personalized, effective, and streamlined healthcare solutions.

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Freely Available, Fully Automated AI-Based Analysis of Primary Tumour and Metastases of Prostate Cancer in Whole-Body [^{18}F]-PSMA-1007 PET-CT

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Highlights:

- A novel AI-based method for detecting and quantifying suspected prostate tumor or local recurrence, lymph node metastases, and bone metastases in ^{18}F-PSMA PET/CT.
- A comprehensive validation process, comparing the AI method with manual segmentations performed by several nuclear medicine physicians, achieving sensitivities on par with human experts.
- The developed AI tool is freely available for researchers and offers potential in standardizing interpretation, acting as a second opinion, and quantifying PSMA-positive tumor burden.

Prostate cancer is one of the most common causes of cancer-related deaths among men worldwide. Accurate staging and discovery of recurrence sites are vital for treatment decisions. PSMA PET/CT is an emerging method for this purpose, but it is subject to inter- and intra-observer variability. The paper aims to address the deficit of nuclear medicine physicians and radiologists able to interpret the studies by developing an AI-based method for detection and quantification of prostate cancer.

The study included 660 patients who were referred for ^{18}F-PSMA PET/CT at Skåne University Hospital in Sweden from December 2019 to December 2020. The images were acquired using a PET/CT, and a diagnostic CT with oral and intravenous contrast was performed for attenuation correction and anatomic correlation. The AI model consists of a Unet3D convolutional neural network (CNN) trained to classify each pixel as either prostate tumor or recurrence, lymph node metastases, bone metastases, or background. The model was trained using image patches, subsets of the full image, and evaluated on a lesion-based level using three sets of expert readers. The study also assessed tumor burden by measuring the total lesion volume (TLV) and the total lesion uptake (TLU).

Sensitivity of the AI method was 79% for detecting prostate tumor/recurrence, 79% for lymph node metastases, and 62% for bone metastases. Nuclear medicine physicians' corresponding sensitivities were 78%, 78%, and 59%, respectively. Correlations of TLV and TLU between AI and nuclear medicine physicians were statistically significant, with Spearman's coefficients of $r = 0.53$ for TLV and $r = 0.83$ for TLU, respectively. The AI-based method was found to be effective in detecting and quantifying suspected prostate tumor or local recurrence, lymph node metastases, and bone metastases, with performance comparable to human experts.

Reviewer's Comments

The study introduces a significant innovation in the field of prostate cancer detection by developing an AI-based method with sensitivity levels comparable to human experts. This freely available tool represents a substantial advancement, demonstrating effectiveness in detecting prostate tumor/recurrence and lymph node metastases, although there is room for improvement in detecting bone metastases. The decision to make the AI tool freely available enhances its accessibility and potential impact.

While further validation using more diverse datasets and improving the sensitivity of detecting low bone metastases remains to be done, this study offers potential applications in treatment evaluation and response assessment through the development of novel AI models, providing a valuable resource for standardization and pointing the way to addressing the lack of experts in the field.

Automated Quantification of PET/CT Skeletal Tumor Burden in Prostate cancer Using Artificial Intelligence: The PET Index

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Highlights:

- A novel AI-based model for automated assessment of PET/CT skeletal tumor burden in prostate cancer, using a CNN.
- A comprehensive dataset of 168 patients from three centers, and the model's performance was found to be superior to using a threshold, correlating moderately strong to physician PET index.
- The developed model offers a consistent and objective evaluation of bone metastases in prostate cancer, potentially paving the way for a new imaging biomarker for skeletal metastases in prostate cancer.

The consistent assessment of bone metastases is vital for patient management and clinical trials in prostate cancer. Previous studies have used various semi-automated methods for quantification, often based on fixed SUV thresholds. These methods are labor-intensive and subject to individual interpretation. This study aims to overcome these limitations by developing a fully automated CNN-based model for calculating PET/CT skeletal tumor burden in prostate cancer patients.

The authors employed manual annotation of skeletal lesions in ^{18}F-fluoride PET/CT scans from 168 patients across three centers to train a CNN for the automated segmentation of lesions. This CNN-based segmentation model is composed of two distinct networks: an organ CNN, which acquires organ masks from CT, and a lesion CNN, which works in conjunction with PET, CT, and organ masks to segment lesions. A quantitative measure of tumor burden is performed by calculating a PET index, which represents the ratio of the resulting segmented lesions to the skeletal volume observed in the images. The training phase utilized 116 patients, while a separate validation set comprised 26 patients. The AI model was then evaluated on an additional 26 patients, and its performance was compared against physician segmentation and an SUV 15 threshold.

The AI model's performance was evaluated through both patient-level and lesion-level analyses. The PET index, representing the percentage of skeletal volume taken up by lesions, was estimated using the AI model, and it correlated moderately strong with the physician PET index (mean Spearman's coefficient $r = 0.69$), while the threshold PET index correlated fairly (mean Spearman's coefficient $r = 0.49$). Sensitivity for lesion detection ranged from 65 to 76% for AI, 68–91% for physicians, and 44–51% for the threshold.

At the patient-level, the AI model's sensitivity was comparable to the readers, but the median PPV was only 52.9%. The AI model did not rule out metastatic uptake in any patient where the readers agreed on prevalence, but it had a higher false positive rate. At the lesion-level, the average number of false positives per patient was higher for the AI model (2.6) compared to the readers (1.5). The AI model's propensity to segment individual lesions as larger volumes and/or due to the higher number of false positives resulted in a generally higher PET index compared to the readers.

Reviewer's Comments

The paper introduces an AI-based model to automate the assessment of PET/CT skeletal tumor burden in prostate cancer. Utilizing CNNs, the study offers a more consistent and objective evaluation, demonstrating moderate to strong correlation with physician PET index and superior sensitivity compared to traditional threshold methods. However, the study's limitations include the need for a more diverse dataset and a broader comparison with different segmentation methods.

Development of an automated AI model for imaging biomarkers heralds a new era in medical diagnostics and treatment. Its potential applicability to different radiotracers and various imaging modalities could open doors for the diagnosis, prognosis, and management of diverse diseases. While the study's limitations call for further refinement and validation in larger, multi-center studies, presenting a developing AI tool that may initiate a transformative era in the utilization of automated biomarkers for a wide range of medical conditions.

Artificial intelligence-based Measurements of PET/CT Imaging Biomarkers are Associated with disease-specific Survival of high-risk Prostate cancer Patients

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Highlights:

- A novel AI-based approach to measure prostate tumor content in PET/CT scans.
- The AI-based measurements of total tumor volume and lesion uptake were significantly associated with disease-specific survival in high-risk prostate cancer patients.
- This approach could offer a more objective and clinically relevant patient stratification and monitoring method compared to conventional measurements.

The study aims to address the limitations of conventional imaging techniques in assessing prostate cancer. Traditional methods depend on subjective visual analysis and readily available metrics such as SUVmax, which might not provide an accurate representation of the disease's activity. The authors hypothesized that AI-based measurements of total volume and lesion uptake of the entire tumor would provide better prognostic significance.

The study utilized an AI-based algorithm trained on 145 patients and tested retrospectively on 285 high-risk prostate cancer patients. The algorithm automatically measured the prostate and its tumor content in PET/CT scans, obtaining data on prostate tumor volume, tumor fraction of the gland, lesion uptake of the entire tumor, and SUVmax. The associations between these measurements, age, PSA, Gleason score, and prostate cancer-specific survival were studied using a Cox proportional-hazards regression model.

To handle multifocal disease, all prostate lesions were considered, including those that were far apart from each other. To avoid false readings due to leakage of uptake from surrounding tissue, Meyer's flooding algorithm was utilized. This method assigns each high abnormal voxel to a local maximum in the PET image, and if this local maximum is found outside the area identified as the prostate, it is classified as leakage and the classification is adjusted to normal.

Out of the 285 high-risk prostate cancer patients who were part of the retrospective study, 23 died of prostate cancer during the follow-up period. The findings revealed that specific factors, including the total tumor volume of the prostate ($p = 0.008$), the tumor fraction within the gland ($p = 0.005$), the total lesion uptake of the prostate ($p = 0.02$), and age ($p = 0.01$), were significantly linked to disease-specific survival. On the other hand, traditional measurements like SUVmax ($p = 0.2$), PSA ($p = 0.2$), and Gleason score ($p = 0.8$) did not show a significant association. The study concluded that the AI-based evaluations were aptly suited for meaningful patient stratification and monitoring in a clinical setting, offering a more precise understanding of individual therapy needs.

Reviewer's Comments

The study unveils an AI-based innovation in prostate cancer diagnosis and prognosis, poised to reshape the way clinicians assess disease-specific survival. This method's effectiveness and sensitivity offer a more intricate understanding of the disease, opening doors to individualized treatment plans. A notable strength of this approach is its ability to handle multifocal disease and the uptake leakage from surrounding tissue. To prevent false readings from uptake leakage from surrounding tissue, Meyer's flooding algorithm was employed, enhancing the accuracy of the measurements.

This research presents a forward-looking perspective on the integration of AI in medical practice. In the past, the interpretation of countless recorded videos was oftern governed by subjective reader judgment. With AI now providing objective imaging biomarkers, medical professionals and researchers can make more informed decisions regarding diagnosis, staging, and treatment procedures. This study serves as a compelling demonstration of AI's potential, paving the way for the development and exploration of more advanced AI-based tools in the future.

Conclusion

The integration of AI into prostate cancer diagnosis and treatment marks a significant advancement. The studies highlighted here demonstrate the potential of AI in detecting and quantifying prostate tumors and metastases with remarkable efficiency and precision. By outperforming traditional methods and offering personalized treatment strategies, these AI-based tools are setting the stage for a new era in prostate cancer management. Future research should focus on further refining these tools to fully realize their revolutionary potential in healthcare.

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Informed Consent As an editorial article obtaining informed consent was waived.

Consent for Publication Not applicable.

Declaration of Generative AI in Scientific Writing I utilized ChatGPT, OpenAI's large language model, primarily to enhance the readability and fluency. However, I meticulously revised and verified the sentences generated by ChatGPT to ensure the content's accuracy and credibility.

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