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Radiomics, PET-PSMA and Machine Learning for Intraprostatic Cancer Diagnosis

Freitas DMO*

Nossa Senhora da Conceição Hospital

***Corresponding Author:** Freitas DMO, Nossa Senhora da Conceição Hospital, Tel.: +5551991424200, E-mail: danielmelecchi@gmail.com

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Abstract

Prostate cancer (Pca) is the second most prevalent malignant neoplasia in man, just after non-melanoma skin cancer. Today, prostate biopsy for tissue sampling is still the gold standard for its diagnosis. However, new generation imaging exam has been used in several clinical scenarios. Yet, positron emission tomography (PET) that targets a specific transmembrane protein on prostatic cells has been studied and changing the natural history of PCa management. Moreover, new software and technologies allow to scan a large amount of imaging features that analyses probability of disease based on exam characteristics called radiomics. In this situation, machine learning may be a inter sting option on investigating possible intraprostatic cancer without previous biopsy conditioned to imaging characteristics and algorithms.

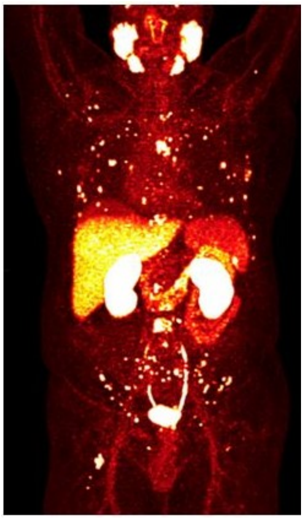

Figure 1: PET-CT PSMA demonstrating target areas with metastasis.

Keywords: Central corneal thickness; Diabetes Mellitus; HbA1c levels; Diabetic retinopathy

Introduction

Prostate cancer (PCa) is one of the most common malignant neoplasms in man. In 2022, more than 60.000 new cases are expected to be diagnosed in Brazil [1]. Transperineal or transrectal ultrasound guided biopsy are both methods for prostate tissue sampling and PCa detection. However,it's not free of complications [2]. After diagnosis, risk analysis and staging are major issues [3]. For example, digital rectal exam and imaging classifies patients in localized, locally advanced or metastatic disease. Additionally, to DRE, Gleason biopsy score and PSA levels are variables used for risk stratification (low, intermediate and high) [1]. As risk increases the probability of metastatic disease also is improved.This is important since treatment strategies changes depending on all these characteristics and variables [2].

Positron emission tomography (PET) is an imaging test that identifies biochemical or metabolic function in tissues [4]. Regarding prostatic neoplasm, the use of PSMA (prostate-specific membrane antigen), a protein found in prostate cancer cells, allows targeting disease in whole body [5]. Firstly, used for biochemical recurrence detection after primary tumor treatment, this imaging exam has been studied for PCA diagnosis and staging in high-risk patients [3].

Although PET-PSMA is extremely accurate for PCa detection its analysis may have an interobserver variability, false-positive results and needs high skilled doctors for exam interpretation [1]. Moreover, recently PET-PSMA has been used for PCa detection without needing prostate tissue sampling previous treatment [6]. In this scenario, the use of artificial intelligence (AI) algorithms has been studied and validated for clinical use. Machine Learning (ML) is a subfield of AI that have been showed significant technological benefits in healthcare [7] With the development of algorithms anddata statistical analysis, models are designed allowing, after input of variables of interest, prediction of a response (output). To be noted, as more the algorithm is used, machine learning will become more accurate in a process of training [7] ML analyses cross-sectional MRI or TC and categorize images relied on pixels using thousands of images for classifier [8]. The results of a large volume of informationanalyzed from images using advanced software is denominated Radiomics [9]. These features are also used during ML build and training. Also, radiomics features may be achieved by different ML algorithms, as random forest, however the data are pre-planned by human decision and if the first decision input is not accurate, all the process will be compromised [9] In this scenario automate prostate imagindgsegmentationnon 3-D architectureusing MRIprovides information about staging and grading [8] In this study, we sought to analyzealgorithms recently used for PET-PSMA interpretation in patients with suspicious PCa.

Methods

We performed a PUBMED searching using the words: "PSMA" and "radiomics" and "machine learning. that resulted in 8 studies. When "algorithm" replaced "machine learning" 8 studies were selected. Only tree studies were about intraprostatic tumor localization. Although PET-PSMA is a promising imaging study for prostate cancer detection there are few studies analizing its accuracy. As long as more data have been achieved, the built of deep learning neural networks using radiomics will provided new perspectives for neolplasm diagnosis.

Discussion

Prostatic malignant neoplasm is a major health issue, not only for its incidence but also for its related costs. PET PSMA is imaging exam that localizes specific tissues in whole body by targeting a protein using a radioactive tracer (the most common is 68Ga-PSMA-11) [4]. Although PSMA radiotracer uptake is stronger in prostate cancer cells, physiology uptake in lacrimal gland, parotids, liver and sympathetic ganglia also occurs [10] Nonetheless, standardized uptake value may vary in different tissues.Moreover, some studies have compared PET-PSMA to histopathologic analysis after lymph node dissection [5,4]. These studies demonstrated a higher specificity for PET, almost 100% [5,9,11]. In addition, PET has been studied to diagnose intraprostatic tumor localization [9], [6] Areas with cancer trend to have a higher SUV when compared to non-cancer prostatic tissue.

The gold standard for PCA diagnosis is still prostate tissue sampling during biopsies, an invasive procedure that may lead to some complications as hematuria and infection [1,2].In this scenario imaging analysis to predict prostate cancer diagnosis is a very interesting issue. ML in heatlhcare has been increased in last year. In respect of prostatic malignant neoplasm, it has been studied in several settings, as intraprostatic tumor localization [17] Papp et al, after analyzing fifty-two patients who underwent PET-PSMA previous radical prostatectomy used these data to perform a ML scheme using random forest classifiers (Monte Carlo cross-validation scheme). In this study the risk for PCa on imaging was predicted using nine random forest [12]. A range between 0.0 and 1.0 was predicted using the model and to avoid overfitting, five features were used for analysis and validation [12] The area under the receiver operator characteristics curve (AUC) of ML prediction between high versus ow risk for prostate cancer was higher (0.86) when compared to conventional imaging exams [12]. The performance of ML demonstrated also a accuracy of 81% and positive predictive value of 88%. In another study Cysouw et al studied prospectively 76 patients with intermediate and high risk PCa. In this trial radiomics were extracted using RaCat software [11]. The authors built a M and used random forest classifier that was trained in 80% of samples. The AUC was used to evaluate ML performance radiomics versus PET-PSMA, the studied showed a AUC of 0.81 for high grade disease in favor of ML radiomics [11].

Although ML seems to be a promising tool for diagnosis in PCa, robust studies are missing to make this technology to be accepted for medical community. In addition, until now, radiomics may evolve with new generation imaging programs and as long as new data will be generated the probability of cancer intraprostatic diagnosis will improve. The benefits of this new technology are multiple. Since until now all prostate cancer are diagnosed by biopsies, the use of ML and radiomics would provide accurate detection without the use of other methods. These could provide a faster diagnosis and treatment decision. To be noted since prostatic tissue sampling may have false-negative diagnosis, ML using radiomics makes easier to located the lesions. However, since the algorithm is built with data input making the decisions tree, this structure must always been reviewed in its formulation [7]. It means that once a wrong decision is made at beginning, all the process will compromised.

In conclusion, ML is a new technology that will change the way healthcare is done nowadays. The right use of medical data to perform MLs that will assist physicians in their clinical routineto make right decisions. In this scenario PET-PSMA seems to be a promising instrument to help on PCa, as the AUC for intraprostatic lesion seems to be higher than the conventional exams. However new studies are needed to proof this theory.

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