



## Why does PSMA PET improve quality of life?

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Radiolabeled prostate-specific membrane antigen (PSMA) positron emission tomography (PET) has completely changed the diagnostic approach for patients affected by prostate cancer (PCa). The available evidence, indeed, demonstrates a strong impact of this imaging modality in different settings of the disease, from diagnosis to the restaging phase [1, 2].

Quality of life (QoL) can be assessed by different types of questionnaires and at different stages of the disease. However, interpretation of final results is inherently subjective and occasionally can be questionable. The minimally important difference (MID) parameter in QoL scores is often evaluated and as such considered useful to clinicians, patients, and researchers. MID often serves as a benchmark for assessing the success of a healthcare intervention. While QoL effects of radiolabeled PSMA agents for therapeutic purposes have been measured in some reports [3–5], similar data for radiolabeled PSMA as a diagnostic tracer is lacking.

With this in mind, it is our opinion the answer to the following question: “Why does PSMA PET improve quality of life?” could be provided in four points: (1) accurate staging and detection, (2) early detection of recurrence, (3) treatment planning, and (4) reduced unnecessary interventions. The first two points are related to the increased diagnostic performance compared to conventional imaging, while the last two points are associated with an effect on therapeutic management.

PSMA PET has shown superior sensitivity and specificity compared to conventional imaging techniques in staging

primary PCa in the proPSMA trial [6] as well as the potential to avoid unnecessary biopsies in selected cohorts of patients when PSMA PET is performed in conjunction with multiparametric magnetic resonance imaging (mpMRI) in the PRIMARY trial [7]. Indeed, accurate staging and detection of lesions can help guide treatment decisions, potentially leading to better outcomes and therefore improved QoL. The proPSMA trial results outlines, in addition to the efficacy in diagnostic performance, that PSMA PET reduces the rate of equivocal findings and radiation exposure. A reduction of equivocal findings determines a lower number of unnecessary additional diagnostic examinations, meaning decreased stress for the patients and a reduced number of hospital visits. Additionally, PCa patients have a relatively good prognosis, requiring many radiological examinations during their lifetime. The opportunity to reduce radiation exposure and cumulative dose may have an indirect effect on QoL. A recent paper by van der Sar et al. [8] reported that 68 Ga-PSMA-11 PET/CT can negatively affect the QoL in primary staging of PCa patients because it can lead to false positive findings in lymph nodes, thus posing a risk of undertreatment, meaning that a patient is treated with palliative intent rather than curative. Significant steps towards standardization and harmonization of PSMA PET reporting have been made by the global nuclear medicine community [9, 10] as well as recommendations by opinion leaders that decision to treat a patient should be made after appropriate multidisciplinary team discussion. Implementation of these measures can improve appropriate decision-making.

PSMA PET is highly sensitive in detecting PCa recurrence at low PSA levels [11, 12]. Early detection of recurrence allows for timely intervention and potentially more effective treatments, which can positively impact QoL by minimizing disease progression and its associated complications. The available literature data about PSMA PET and QoL are scarce, and only three papers are currently available. However, in all the reports, PSMA PET is a useful tool that guides selective radiotherapy planning with a subsequent beneficial effect or stability on QoL (Table 1). PSMA PET findings were used to modulate different stereotactic

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**Table 1** Characteristics of the studies including QoL evaluation

Authors, ref	Phase trial	N of pts	Primary end-point	Questionnaire for QoL	Effect on QoL
Bowden et al., [13]	II	92	To evaluate outcomes for men with biochemically recurrent PCa who were selected for transponder-guided SRT to the prostate bed alone by 68 Ga-PSMA-PET	-SF-12, vrs 1 -EPIC-26	No changes
Lucchini et al., [14]	Observational	30	To investigate the feasibility of ultra-hypo fractionated RT to the prostate bed in patients with biochemical and/or clinical relapse following RP	-ICIQ-SF -EPIC-CP	No changes
Greco et al., [15]	II	30	To explore whether prostate motion mitigation using the rectal distension-mediated technique is safe and effective in SABR salvage treatment of intraprostatic cancer recurrences following initial RT for primary PCa	-IPSS -EPIC-26	No changes after 3 months from therapy

NA not available, PCa prostate cancer, sRT salvage radiotherapy, SF-12 Short Form 12, EPIC-26 Expanded Prostate Cancer Index Composite, ICIQ-SF International Consultation on Incontinence Questionnaire-Short Form, CP clinical practice, RT radiotherapy, SABR stereotactic ablative body radiation, IPSS International Prostate Symptom Score

body radiation therapy (SBRT) dosages (70 and 74 Gy, respectively in the case of a negative or a positive scan), in a phase II trial enrolling 92 patients who underwent SBRT alone after radical prostatectomy (RP) [13]. No statistically significant difference in the physical component summary or mental component summary scores from baseline to 3 years post-treatment was reported [13]. Similarly, PSMA PET was used after RP and after RT in two different populations of 30 patients, for guiding to SBRT or stereotactic ablative body radiation (SABR) [14, 15], respectively. Lucchini et al. [14] concluded that SBRT guided by PSMA PET did not increase the short-term toxicity or determine a significant decline in QoL. Conversely, the QoL questionnaires in patients treated with a PSMA-guided reirradiation after a primary RT demonstrated a transient worsening in urinary function but a stable condition after 3/18 months [15].

PSMA PET can help identify the extent and location of PCa lesions, which can assist in treatment planning. Precise information about the disease burden can help tailor treatment strategies, such as focal therapies or targeted RT, potentially reducing side effects and preserving QoL. The impact of PSMA PET on patient management has been widely demonstrated in different settings of the disease, reaching 52% in the case of biochemical recurrence [16, 17]. PSMA PET can also help distinguish local recurrence from distant metastases which can then tailor appropriate treatment approaches. By accurately identifying the location and extent of the disease, unnecessary interventions and their associated side effects can be avoided, contributing to a better QoL. As largely reported, QoL is often severely affected by androgen deprivation therapy (ADT) [18]. The decision to initiate castration therapy in apparently healthy men has far-reaching consequences regarding toxicity and QoL issues. In example, a high level of fatigue

is seen in patients after curative radiation and long-term ADT [19]. The efficacy of PSMA in establishing the presence of oligometastatic disease [20, 21], thus allowing for the postponement of ADT, can be considered an important piece of the puzzle for improving QoL in PCa patients.

In summary, PSMA PET can provide a more accurate assessment of clinically relevant disease, avoid unnecessary interventions, guide appropriate therapeutic management, and monitor response to treatment. All of these abilities can alleviate anxiety and uncertainty in patients. Therefore, PSMA PET results may provide reassurance or prompt appropriate action, leading to better psychological well-being and overall QoL.

There are indeed ongoing challenges that need to be addressed in order to further improve QoL for PCa patients: (1) cost considerations and accessibility of PSMA PET; (2) standardization and evolving guidelines for PSMA PET utilization, mainly addressing the effects on QoL (i.e., better knowledge of correct questionnaires focusing on QoL); and (3) research advancements and potential future applications. As research continues to evolve and accessibility improves, it is crucial for healthcare professionals to embrace this technology and its impact on improving the QoL of PCa patients.

## Declarations

**Ethics approval** Institutional Review Board approval was not required because the paper is an Editorial.

**Informed consent** Not applicable.

**Conflict of interest** The authors declare no competing interests.

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