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Editorial Open Access

Rationale for Clinical Use of 11C-Choline PET/CT in Prostate Cancer Patients

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Editorial

Prostate cancer is the most frequent cancer among older men, with a critical impact in social, sanitary and economic grounds for Western societies. Imaging techniques have proved useful for disease staging, for determining disease volume in terms of a better therapeutic approach, as well as for re-staging after disease recurrence [1].

Early diagnosis of prostate cancer relies on serum concentration of total prostate–specific antigen (PSA), digital rectal exam and trans rectal ultrasound of prostate. Once clinical-analytical suspicion of prostate cancer is arised, trans rectal ultrasound guided biopsy allows for histo pathological confirmation. Prostate biopsy is the gold standard in tumor characterization [1-4].

Disease staging prior to any therapeutic approach relies on a combination of different imaging techniques. Lymph node involvement is assessed by CT or MRI, with sensitivity values ranging between 60-70%. This not very high sensitivity is due to the fact that radiology diagnosis depends on morphometric criteria, and especially on the size of lymph nodes. Bone involvement is routinely assessed by means of the bone scan, with high sensitivity results, but low specificity (50%, approx.). MRI imaging is superior to bone scan, however whole body is not routinely scanned in MRI [1,2,5-8].

The therapeutic approach in prostate cancer, thus with palliative or radical aim, depends on how aggressive local tumor is (Gleason score), as well as on disease spread (TNM, PSA, Roach formula) [1-4].

After radical treatment of prostate cancer has been performed and disease recurrence is suspected clinically or by a PSA increase, several known procedures are implemented to localize and evaluate disease spread, and results of which will delineate the new therapeutic approach suitable in these patients. Bone scan and CT are also used for determining bone and lymph involvement respectively, likewise in the primary tumor staging. Transrectal ultrasound is used for guiding biopsy in the prostatic bed, as well as for lymph node evaluation. MRI performance is similar to CT, with its accuracy being improved with the aid of the spectroscopy information [5-10].

However, in many patients, and despite of applying all the available diagnostic procedures, disease location remains unsuccessful and therefore real disease spread is not available for their accurate clinical management [8].

Metil-11C-Choline (11C-Choline) was first introduced by Hara et al. as a new PET tracer for oncology imaging. 11C-Choline shows a high affinity for proliferative tissue. Its uptake mechanism depends on phospholipid biosynthesis, which is a critical compound found in cell membranes. Since carcinogenesis is characterized by a high cell proliferation rate, a high phospholipid concentration is expected in malignant tissues, and consequently, a high 11C-Choline uptake. The amount of 11C-choline transporters also plays a role in uptake process of 11C-Choline, although the exact mechanism underlying is still under investigation. 11C-Choline PET has been reported to be useful for studying several tumours with high tumor/background signal ratio, even in slow tumor growth kinetics and/or well differentiated lesions like prostate cancer, broncho alveolar carcinoma, low grade glioma and meningioma, which all may be undetectable with 18F-FDG PET. Moreover, the 11C-Choline holds a high tumour/background ratio in those lesions located in pelvis, since there is no tracer excretion in urinary pathway, as opposed to 18F-FDG, in which urinary physiological elimination obscure the prostate area [11].

Several studies have reported 11C-Choline uptake in primitive tumours as well as its metastases in patients with prostate cancer. Results are, however, controversial with respect to primitive prostate tumour since 11C-Choline uptake is also found in normal prostate tissue. Hara et al. suggest that semi-quantification algorithms with SUV (Standard Uptake Value) may improve accuracy of PET imaging, since SUV values found in prostate cancer were always higher than those found in normal prostate tissue as well as in benign hyperplastic tissue. However, these findings have not been validated in further patient series [12-14].

11C-Choline has been reported a good efficacy for detection of lymphadenopathies or bone metastases in staging of primitive prostate tumour. In a large prospective study made with patients with lymph involvement, Jong et al. found sensitivity, specificity and accuracy values for 11C-Choline PET to be of 80%, 96% and 93%, respectively. In this series, 11C-Choline PET sensitivity was superior to CT and MRI. Bone involvement in prostate cancer is routinely imaged with a bone scan, although several cases of bone marrow involvement have been reported to be negative with bone scan and positive with 11C-Choline PET [1,5-9].

In the clinical setting of radical treatment for prostate cancer, 11C-Choline PET may also be of great interest for clinical suspicion of recurrence, or when levels of PSA are sustainably increased. This interest becomes clinically critical when conventional imaging methods are negative or inconclusive for the detection of recurrence. The absence of prostate tissue allows for a better detection of local and regional recurrence. 11C-Choline PET has been useful for those patients in whom recurrence is suspected but has not been located with conventional imaging methods [1,5-9].

The possible relationship found between sensitivity for the detection of recurrence with 11C-Choline and serum levels of PSA is still under debate. Several authors consider that sensitivity is acceptable for PSA levels above 4 ng/ml. Results are especially controversial for values between 1 and 4 ng/ml. The adequate PSA threshold that may allow for a high probability of a positive 11C-Choline PET study remains to be determined. Catellucci et al demonstrate an improve selection of patients with rising PSA low than 1 ng/ml related with PSA doubling

time (PSAdt) allowing early diagnosis of recurrence and potentially treatment strategy [8,15].

In the clinical setting of localizing and restaging a recurrence from a prostate cancer already treated, a positive 11C-Choline PET study leads to the histopathological confirmation, and also allows to introduce an adequate therapeutic approach. A negative 11C-Choline PET study directs to a close clinical and diagnostic imaging follow-up [1,8].

The main shortcoming of 11C-Choline lies in the short radioactive half-life of 11C (20 min.), which prevents from its use in those PET facilities with no cyclotron availability. Choline tracer labelled with 18F may be a feasible alternative, but its urinary elimination, similar to 18F-FDG, make therefore pelvic imaging interpretation difficult [16].

The emergence of new PET/CT technology increases significantly the diagnostic and clinical yielding of PET imaging, thus better localizing 11C-Choline deposits as well as determining its anatomical boundaries more precisely, and therefore reducing the false-positive rates [1].

An ultimate indication of 11C-Choline PET/CT in prostate cancer may be for volume planning in the radiotherapy setting, which is especially important with the implementation of new radiation techniques like the modulated radiotherapy and image-guided radiotherapy [17,18].

In conclusion, the main clinical indications of 11C-Choline PET imaging are as follows:

- Disease staging in patients diagnosed with medium/high risk prostate cancer: T3-4 and/or Gleason score 8-10 and/or PSA >20 ng/ml and/or >25% of probability of lymphatic involvement according to Roach formula.
- Patients with radical treatment of prostate cancer and increase in PSA levels with conventional imaging negative or inconclusive (selection patients based in threshold PSA and PSAdt).

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