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Experience with Fluoromethylcholine-(18F)

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The main limitation to the routine use of choline-(11C) or acetate-(11C) is the short physical half life of carbon-11 (20 minutes) that requires a cyclotron in the close vicinity of the PET centre. Several choline analogues labelled with fluorine-18 has been developed to circumvent this logistical limitation. Fluoromethylcholine-(18F) or FCH (1) has been the most widely used, as its biodistribution is rather similar to that of choline-(11C), even though its urinary excretion is greater (2). Acquisition of early PET/CT images of the pelvis (preferably dynamic acquisition from 1 to 8 min post injection) allows the visualisation of abnormal uptake in the prostate bed or the pelvic lymph node basins before high urine activity enters the ureters and the urinary bladder. The same team demonstrated the superiority of FCH over FDG to detect prostate cancer tissue, regardless to its dependence to androgens (3).

Detecting cancer inside the prostate gland and guiding biopsy for its assessment

Kwee (4) demonstrated on biopsy specimens that FCH uptake was significantly greater in pathologic prostate tissue than in healthy tissue. But this increase in FCH uptake was not specific for cancer tissue and was also observed in benign hypertrophy or in prostatitis. In series of 17 patients, 6 patients had strictly unilateral cancer and FCH PET/CT accurately showed which prostate lobe was harbouring cancer. However, Schmid (5) reported that an exact correspondence between FCH PET/CT anomalies and cancer tissue was observed only in 1 of 9 patients who underwent radical prostatectomy. To enhance specificity, Kwee (6) then proposed dual time point imaging at 7 min and 60 min after re-voiding : in 26 patients, FCH uptake increased with time in malignant prostate lesions and decreased in benign lesions. Recently, the same team reported results of the analysis of 90 prostate sextants in 15 patients who underwent FCH PET prior to radical prostatectomy (7). In 13 patients, the sextant with the highest SUVmax corresponded to the largest tumour in the specimen. The team in Klagenfurt recently reported on FCH PET/CT performed in 20 such patients (8) : in 5 patients, FCH PET/CT allowed the identification of neoplastic lesions. Complementary information was derived from this study : semiquantitative analysis with SUVmax and dual-phase acquisition protocol were not helpful in the discrimination of malignancy.

Primary staging of prostate cancer and determination of the biological tumour volume for radiotherapy

The drawbacks of FCH PET to localise cancer tissue inside the prostate gland have been reported in the previous paragraph : limited sensitivity for small lesions in multifocal cancer and limited specificity due to uptake in benign lesions. Nevertheless, the team in Zurich considered that FCH PET/CT might serve for semi automatic segmentation for radiotherapy of prostate cancer (9). Concerning the detection of distant cancer metastases, FCH PET/CT could be helpful, in particular in a subgroup of patient at risk for such a spread : initial Gleason score > 7 or PSA serum level > 10 ng/mL or a doubling time of PSA serum levels < 3 months. In series of 49 such patients, Langstger (10) reported a 4% rate of downstaging (unconfirmed suspicion of bone metastases) and a 16% rate of upstaging (unexpected bone metastases in 4 cases and multiple lymph node metastases in 2 cases) with an impact on management. In the study of Hacker (11) who used sentinel node histology as the standard of truth, FCH identified all lymph node metastases of a size greater than 8mm. These results were recently confirmed by the team in Zurich in 43 patients referred for initial staging (12) : on a per patient basis, there was 1 true positive case vs. 4 false negative case for the detection of lymph node metastases while all 4 cases of bone metastases were true-positive. In summary, FCH PET seems to be useful in the pre-treatment staging of high risk prostate cancer to warn for unknown distant spread (13), but cannot rule out a minimal invasion of the contiguous organs (seminal vesicles) or of regional lymph nodes.

Search for recurrence

This setting seems to be the most promising for FCH PET/CT in prostate cancer. In preliminary series of 9 patients presenting with a biochemical recurrence (isolated rising serum PSA levels, 14 ng/mL on average at FCH imaging), FCH PET/CT brought in evidence in 3 cases an isolated local recurrence, in 4 cases no local recurrence but lymph node invasion which was checked by histology and confirmed in 2 cases, in 1 case both localisations, and in the final case bone metastases which were also visible on bone scintigraphy (5). It has subsequently been shown by the team in Linz that recurrent prostate cancer could be detected on FCH PET/CT even when serum PSA levels were less than 5 ng/mL (14) : a true positive result was obtained in 41% of the 17 patients. In the already quoted study from Zurich (12), 68 patients were referred for restaging, and 57 had pathological FCH accumulation. Overall sensitivity to detect recurrent disease was 86% and 71% when serum PSA levels were less than 2 ng/mL. The team in Aviano studied 100 patients with suspected recurrent disease (15). Recurrence was detected on FCH PET/CT in 54 patients with mean serum PSA levels of 48 ng/mL. In contrast in 46 patients FCH PET/CT did not show any anomaly and no other imaging modality was able to detect recurrent disease in any of them during a 6 month follow-up ; their PSA serum levels were much lower (2 ng/mL on average). The intensity of the uptake by some bone metastases increased with time which could justify the acquisition of delayed images (60 min) when the early images are negative.

Our experience on 106 FCH PET/CT which were performed for suspicion of prostate cancer recurrence (16), is that high PSA absolute velocity permitted to pinpoint patients with PSA levels < 5 ng/mL in whom FCH PET/CT was subsequently positive, while relative PSA velocity was of no help.

Therapy monitoring and interference

To the best of our knowledge, there is currently no data available on the early evaluation with FCH PET of hormonal treatment or chemotherapy. The detection of persistent disease is possible and useful when no significant drop in PSA serum levels is observed after local therapy ; such a case has been illustrated by our team (17-fig 5).

The team in Geneva performed FCH PET/CT in 11 patients who had low but significant PSA serum levels, between 0.08 and 0.76 ng/mL, after radical prostatectomy and were scheduled for adjuvant or salvage radiotherapy (18). Foci of local recurrence were visible in 5/11 patients with no distant lesion while endorectal MRI was locally positive in 10. Authors do not recommend FCH PET/CT as a standard diagnostic tool for early relapse or suspicion of minimally persistent disease after surgery. The performances of acetate-(11C) determined in a parallel group were not clearly superior.

Concerning anti-hormone treatment, in our experience, when serum PSA levels are high enough during anti-hormone treatment, it is not justified to interrupt the treatment to perform FCH PET/CT. In the series of 68 patients referred for biological recurrence reported by Husarik (12), 13 were receiving anti-hormone therapy and only 2 of their examinations did not show any pathological FCH accumulation. Sensitivity at any PSA level was 84% in patients with anti-hormone therapy, similar to 83% without anti-hormone therapy.

Conclusion

In conclusion, FCH PET/CT could become a major tool in case of biologic recurrence of prostate cancer to detect early and accurately bone and/or visceral involvement. For the same reason, it could be clinically useful for the initial staging of advanced prostate cancer, essentially in search for distant metastases, since results for initial N staging were "discouraging" (12). Its impact on patient management in these settings has still to be assessed and quantified. Its role (if any) in guiding prostate biopsy to assess cancer, helping to determine radiotherapy target volumes and early therapy evaluation remains to be evaluated in comparison with other imaging modalities, in particular endorectal MRI with diffusion.

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