

THE WAR IS OPENED: PSMA VS. $^{64}\text{CuCl}_2$ VS. CHOLINE PET/CT

Laura Evangelista¹ and Fabio Zattoni²

¹Nuclear Medicine and Molecular Imaging Unit, Veneto Institute of Oncology IOV – IRCCS, Padua, Italy

²PhD Course in Clinical and Experimental Oncology and Immunology, Department of Surgery, Oncology, and Gastroenterology, University of Padua, Padua, Italy.

Dear Editor,

I have read with a great interest the paper by Piccardo et al (1) and the editorial by Ceci et al (2) recently published in your journal.

By a careful analysis of the published data some comments seem necessary.

First, a specific ^{18}F -Choline acquisition protocol would improve the detection of recurrent prostate cancer, either for prostatic fossae and for lymph nodes. PET acquisition time after only 20 min from ^{18}F -Choline injection, as reported by the authors (2) cannot be considered as a standard. In a recent review, 21/29 (72%) studies, focused on ^{18}F -Choline PET or PET/CT, reported a late (after 60 minutes) whole-body (WB) scan, while only 8/29 (28%) reports after 10-15 minutes after tracer injection (3). In our recent experience (4) performed in 75 patients who underwent both an early static and late WB acquisition, we found that in case of low PSA levels (< 2 ng/mL), early ^{18}F -Choline PET/CT scan detects recurrent disease in prostatic fossae, in 15 subjects. Conversely, late images were positive only in 4 patients. Therefore, a specific acquisition protocol would be useful to improve the detection rate until to 70%, in case of prostatic fossae recurrence. Furthermore, Oprea-Lager et al (5) reported that a single time-point standardized uptake value (SUV) measurements, 30 min post-injection, is a reasonable alternative for predicting the enlarged pelvic lymph nodes. However, no dedicated European guidelines are now available for ^{18}F -Choline PET/CT examination.

Second, the authors did not report any data about $^{64}\text{CuCl}_2$ acquisition that they have used (early, after 4h or late, after 24h) for the interpretation of the images. This information would be useful for the repeatability of the study and also for understanding the correct schedule of patients.

Third, the comments by Ceci et al (2) are mainly focalized on the comparison between $^{64}\text{CuCl}_2$ and prostate specific membrane antigen (PSMA)-based radiopharmaceuticals. The majority of available data about PSMA-directed PET are made with ^{68}Ga -PSMA-11, it means with a radiopharmaceutical agent that has a urinary excretion, therefore associated with a loss of information for prostatic fossae recurrence. A study performed by Uprimny et al (6), reported that performing an early (after 4-8 min) and late (after 60 min) ^{68}Ga -PSMA-11 PET/CT acquisition, an early ^{68}Ga -PSMA-11 scan was able to identify the presence of prostatic fossae recurrence in 50 patients, with a gain of detection rate more than 50% than late acquisition. Again, the acquisition protocol is useful for the correct interpretation of PET/CT findings.

In our opinion, the comparison between $^{64}\text{CuCl}_2$ and ^{68}Ga -PSMA-11 or ^{18}F -Fluciclovine is mandatory, however:

- A specific end-point should be drawn, in order to assess the impact on the patients' management and consequent survivorship rather than only detection rate.

- A final pathology as a gold standard should be recommended in order to solve the problematic gap between imaging and the pure biochemical recurrence and to prove the new tracers reliability. However, it should be recalled that salvage lymph node dissection is still experimental and trans-rectal ultrasound-guided biopsy of the vesicourethral anastomosis is no more recommended by the European Association of Urology (EAU) and National Institute for Health and Care Excellence (NICE) guidelines.

However, we have taken in mind that although a long half-life, the image resolution of $^{64}\text{CuCl}_2$ is significantly better than ^{11}C and ^{68}Ga (7). This characteristic has an important benefit on the identification of small areas of prostate cancer recurrence, particularly in case of local recurrence after radical prostatectomy.

REFERENCES

1. Piccardo A, Paparo F, Puntoni M, Righi S, Bottoni G, Bacigalupo L, et al. $^{64}\text{CuCl}_2$ PET/CT in Prostate Cancer Relapse. *J Nucl Med*. 2018; 59:444-451.
2. Ceci F, Fendler W, Eiber M. A New Type of Prostate Cancer Imaging: Will $^{64}\text{CuCl}_2$ PET/CT Flourish or Vanish? *J Nucl Med*. 2018;59:442-443.
3. Evangelista L, Cervino AR, Guttilla A, Zattoni F, Cuccurullo V, Mansi L. ^{18}F -fluoromethylcholine or ^{18}F -fluoroethylcholine pet for prostate cancer imaging: which is better? A literature revision. *Nuclear Medicine and Biology* 2015; 42:340–348.
4. Zattoni F, Cattaneo F, Zattoni F, Evangelista L. MP77-09 EARLY AND LATE IMAGES OF ^{18}F -CHOLINE (FCH) PET/CT FOR THE DETECTION OF PROSTATIC FOSSAE RECURRENCES IN PROSTATE CANCER WITH A BIOCHEMICAL FAILURE (PSA > 2 NG/ML). *J Urol* 2018; 199: e1030-e1031.
5. Oprea-Lager DE, Vincent AD, van Moorselaar RJ, Gerritsen WR, van den Eertwegh AJ, Eriksson J, et al. Dual-phase PET-CT to differentiate ^{18}F Fluoromethylcholine uptake in reactive and malignant lymph nodes in patients with prostate cancer. *PLoS One*. 2012;7:e48430.
6. Uprimny C, Kroiss AS, Fritz J, Decristoforo C, Kendler D, von Guggenberg E, et al. Early PET imaging with ^{68}Ga -PSMA-11 increases the detection rate of local recurrence in prostate cancer patients with biochemical recurrence. *Eur J Nucl Med Mol Imaging*. 2017;44:1647-1655.
7. Bunka M, Müller C, Vermeulen C, Haller S, Türlér A, Schibli R, et al. Imaging quality of ^{44}Sc in comparison with five other PET radionuclides using Derenzo phantoms and preclinical PET. *Applied Radiation and Isotopes* 2016; 110:129–133.