Clinical and Translational Imaging (2018) 6:69–71
https://doi.org/10.1007/s40336-018-0262-2

SPOTLIGHT

# PET/CT and urinary cancers: the message from urologists

**Fabio Zattoni**[1,2] · **Ryan A. Hankins**[3]

Received: 25 October 2017 / Accepted: 4 January 2018 / Published online: 25 January 2018


PET/CT technology implementation is taking off notably in clinical oncology and its capabilities have become quite well known among imaging specialists and referring physicians, however, its full adoption among urologists has not yet been achieved. Although, English publications on "PET" and "Urology" are exponentially increasing, the majority of them are dealing with prostate cancer, and only a few studies focus on renal and transitional cell carcinoma. Therefore, due to several limitations in the available literature in urology, the current European and American Urology Guidelines suggest the use of PET/CT in oncologic patients only in a very selected subgroup. The appropriate use of PET/CT is still an underutilized tool in the urologists' armamentarium in particular for those cancers developing from the urinary system. However, as shown by promising evidence [1], it is time to reconsider PET/CT to solve clinical needs still unresolved in tumors such as kidney and urothelial cancers, UC (Table 1).

## Kidney cancer

The ability to correctly determine tumor histology of small renal masses without using biopsy is an interesting field of study in renal cancer. Preliminary research on $^{18}$F-FDG PET/CT highlighted the potentials of this technology to differentiate clear cell carcinoma from other tumor types. In particular, $^{18}$F-FDG PET/CT seems to differentiate clear cell carcinomas from less aggressive phenotype or different Fuhrman grade avoiding the use of a percutaneous kidney biopsy [2]. This could guide surgeons in their surgical approach or modify clinical decisions, especially when active surveillance is considered. As a total body scan, PET/CT can also be used for local and distant recurrence. $^{18}$F-FDG PET/CT may be useful in distinguishing fibrosis following surgery to local relapse. Furthermore, in advanced kidney cancer, new evidence supports the use of PSMA-targeted PET/CT for the accurate detection of the metastases [3]. The adoption of this technology may be used as guide for a complete resection of the oligometastatic site or a stereotactic treatment in case of spinal metastasis. This ideally will improve survival, delay systemic therapy and improve symptoms control.

As a new frontier, antibodies radiolabeled with positron-emitting radionuclides may allow an Immuno-PET with an in vivo quantification of the efficacy of targeted therapies. Interestingly, PSMA is expressed in the neovasculature and many of the commonly used drugs for this disease target angiogenesis. Thus, PSMA-targeted PET/CT may play a role in the selection of patients' therapy, the prediction of response to systemic medications and an in vivo assessment of the efficacy of therapies. A timely diagnosis of not responder to targeted therapies may facilitate early switch to a second or third line therapy and as a consequence, improve survivorship. Certainly, in metastatic renal cell carcinoma a more accurate prognostic tool with functional imaging is desiderative for patient stratification within trials for new targeted drugs [4].

## Transitional cell carcinoma (TCC)

$^{18}$F-FDG PET/CT is unlikely to add clinical utility in staging the primary TCC. Conventional CT urogram, urine cytology and simple cystoscopy and/or ureterorenoscopy in almost all cases are able to correctly stage the tumor within the urinary tract. Studies on $^{18}$F-FDG PET/CT show conflicting results, but agree on the several advantages of this tool in comparison to conventional imaging: (1) it combines anatomical and functional imaging (2) less contrast allergy than iodine based contrast, (3) and avoids

✉ Fabio Zattoni
fabiozattoni@gmail.com

1 Urology Unit, Academic Medical Centre Hospital "Santa Maria della Misericordia", Udine, Italy

2 Clinical and Experimental Oncology and Immunology, Department of Surgery, Oncology, and Gastroenterology, University of Padua, Padua, Italy

3 Medstar Georgetown University Hospital, Washington, DC, USA

**Table 1** A schematic summary of the needs of clinicians, the potential role of imaging and its implications for kidney cancer and transitional cell carcinoma

| | Possible needs of clinicians | Clinical implications of a positive imaging |
|---|---|---|
| Kidney cancer | Ability to correctly determine tumor histology of small renal masses | Avoid kidney biopsy<br>Drive surgeons in their surgical approach or modify clinical decisions (active surveillance versus surgery) |
| | Follow-up after surgery | Improved detection of local relapse after surgery<br>Early start of medical therapies |
| | Accurate detection of metastases | Complete resection of the oligometastatic site or stereotactic treatment in case of spinal metastasis |
| | Patient selection for targeted therapy<br>Evaluation after systemic therapy<br>In vivo assessment of targeted therapy with a PET imaging quantification of antibodies radiolabeled with positron-emitting radionuclides. | Improve prognosis<br>Patient's selections to an appropriate medical therapy<br>Timely diagnosis of not responder may facilitate early switch to a second or third line drug |
| Bladder cancer<br>Upper tract urothelial carcinoma | Lymph node assessment | Neoadjuvant chemotherapy<br>Immediate surgery<br>Guide the extent of lymphadenectomy |
| | Evaluation of recurrence after surgery | Decide for adjuvant chemotherapy |
| | Evaluation of response after systemic therapy | Decide for second/third line chemotherapy |

acute renal insufficiency in patients at risk of long term renal impairment.

Clinicians expect a new imaging technique to provide a reliable assessment of lymph node and distant metastasis in TCC. This can be useful for the correct patient selection for surgery or medical therapy. Currently, clinical lymph node staging is based on dimensional criteria which can miss minimal, but significant tumor involvement. Unfortunately, $^{18}$F-FDG PET/CT before radical cystectomy has a low sensitivity in detecting and localizing regional lymph node metastasis. Thus, lymph node dissection is still a central part of the radical cystectomy for its staging and curative intent. For upper tract urothelial carcinoma the beneficial intent of lymph node dissection is itself under debate. The problem lies in conventional imaging's inability to discriminate between patients with high risk of lymph node involvement. $^{18}$F-FDG PET/CT for lymph node involvement in upper tract TCC does not exceed 60%. Further studies are needed to better address this topic and compare the extension of lymphadenectomy with $^{18}$F-FDG PET/CT results in a per lesion analysis [5]. Regarding the evaluation of recurrence after primary treatment, in a recent retrospective study with more than 280 patients, PET/CT was proven to have a good accuracy for both bladder and upper tract urothelial carcinoma in a per patient-based analysis. In addition, in a per site-based analysis, FDG PET/CT showed a higher accuracy than conventional imaging in lymph node assessment [6]. From a clinical stand-point, these findings have important implications in the follow-up after primary treatment and in therapeutic decision-making of UC recurrences. Finally,$^{18}$F-FDG PET/CT may provide crucial information about the response to chemotherapy or immunotherapy in UC, an area where other methods are generally inadequate.

It is well known that a possible limitation of $^{18}$F-FDG PET/CT in UC is the physiologic urinary excretion of 18F-FDG and the need of diuretics post-hyperhydration in the assessment of recurrence. However, to further improve patient selection and risk stratification, the use of a co-registration CT urography with PET/CT could be encouraged for better staging of UC recurrence in either the residual urinary tract after surgery and in the lymph nodes. In fact, the continent or incontinent urinary diversion may alter the detection rate of retroperitoneal or pelvic lymph nodes. Indeed, the intense intraluminal urine activity can hinder the detection of an adjacent small local recurrence or metastatic lesions. Thus, stratification according to the urinary diversion may improve the staging of retroperitoneal and pelvic lymph nodes.

## Comments

Definitive applications of PET/CT in urinary cancers are still missing. Indeed, current literature has several limitations. There is a lack of prospective and adequately powered studies with homogeneous population. The comparison of different imaging modalities often uses inappropriate Gold standards. Furthermore, health economic considerations are often undervalued over the sensitivity and specificity of an imaging test. However, our daily practice has open questions still unsolved. So, we are looking foreword to seeing if new diagnostic modalities, like PET/CT, may really change our practice.

We prospect great changes in the use of PET/CT for kidney cancer and TCC. Fusion Images (i.e.: PET/CT with urography phase of the CT scan) will be able to better define the classic anatomical images by combining functional and metabolic outcomes. This will enhance the guidance of site-directed therapy (i.e., surgical metastasectomy, stereotactic ablative radiotherapy, augmented reality surgery). In a not so improbable view of the future, new tracers with diagnostic and curative intent would directly treat tumors with an essential change in the treatment path of urologic malignancies.

## Compliance with ethical standards

**Conflict of interest** Authors declare no conflict of interest.

**Human and animal rights statement** This article does not contain any studies with human or animal subjects performed by any of the authors.

## References

1. Tagliabue LMS (2016) Time to reconsider FDG-PET/CT for local and distant staging of urological malignancies. Clin Transl Imaging 4:221–223
2. Nakajima R, Nozaki S, Kondo T, Nagashima Y, Abe K, Sakai S (2017) Evaluation of renal cell carcinoma histological subtype and fuhrman grade using 18F-fluorodeoxyglucose-positron emission tomography/computed tomography. Eur Radiol 1:1–8
3. Gorin MA, Rowe SP, Hooper JE, Kates M, Hammers HJ, Szabo Z et al (2017) PSMA-targeted 18F-DCFPyL PET/CT imaging of clear cell renal cell carcinoma: results from a rapid autopsy. Eur Urol 71:145–146
4. Alongi P, Picchio M, Zattoni F, Spallino M, Gianolli L, Saladini G et al (2016) Recurrent renal cell carcinoma: clinical and prognostic value of FDG PET/CT. Eur J Nucl Med Mol Imaging 43:464–473
5. Zattoni F, Evangelista L, Guttilla A, Zattoni F (2016) Radiolabelled choline and FDG PET/CT: two alternatives for the assessment of lymph node metastases in patients with upper urinary tract urothelial carcinoma. Eur J Nucl Med Mol Imaging 43:576–577
6. Zattoni F, Incerti E, Colicchia M, Castellucci P, Panareo S, Picchio M, Fallanca F, Briganti A, Moschini M, Gallina A, Karnes JR, Lowe V, Fanti S, Schiavina R, Rambaldi I, Ficarra V, Evangelista L (2018) Comparison between the diagnostic accuracies of 18F-fluorodeoxyglucose positron emission tomography/computed tomography and conventional imaging in recurrent urothelial carcinomas: a retrospective, multicenter study. Abdom Radiol (NY). https://doi.org/10.1007/s00261-017-1443-6