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# Dual Time F-18 FDG PET/CT Imaging in the Diagnosis of Renal Cell Cancer

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**Abstract:**

**Background:** There are conflicting results in estimation of primary renal tumors by F-18 FDG PET/CT in the literature. Aim of this study is to evaluate diagnostic efficiency of F-18 FDG PET/CT and dual time imaging in the diagnosis of renal cell cancer.

**Methods:** Dual time F-18 FDG PET/CT examinations of 17 patients (55.2 ± 9.9 years old; 7 F, 10 M) with prediagnosis of renal cell cancer were retrospectively evaluated. All of the patients underwent operation and histopathological results were compared with PET/CT results. In order to compare numerical variables Kolmogorov-Simirnov, Mann Whitney U and Paired samples T tests were performed in SPSS version 15.0 and $p<0.05$ considered statistically significant.

**Results:** Among 17 patients 15 patients were confirmed to have renal cell carcinoma, 2 patients had benign pathologies (oncocytoma, metanephritic adenoma). According to the early phase analysis, the sensitivity, specificity, accuracy, positive and negative predictive values of PET/CT regarding diagnosis of primary tumor were 20%, 100%, 29%, 100% and 14%, respectively. Additionally the difference between SUVmax values in the early and the late phase was not statistically significant ($p>0.05$).

**Conclusion:** Since only the positive predictive value of PET/CT is sufficiently high and the sensitivity is very low, diagnosis of renal tumors by F-18 FDG PET/CT is not an accurate method. In addition, dual-phase imaging in the diagnosis of renal cell cancer has no benefit.

**Keywords:** Dual phase imaging, F-18 FDG, PET/CT, renal cell cancer, renal tumor, SUV.

## INTRODUCTION

Renal cell cancer is predominantly presented in seventh decade of life and frequency of this tumor in developed countries rises progressively in aging population [1]. Since computed tomography (CT), positron emission tomography/computed tomography (PET/CT) and magnetic resonance imaging (MRI) are addressed in more patients recently, incidental renal tumors are more frequently diagnosed [2]. Although there are some criteria about the estimation of the renal masses by CT by a renal CT protocol, unfortunately there are borderline tumors regarding radiological imaging [3]. Biopsy of renal tumors is not preferred due to the invasive character of the method and fine needle biopsy is not preferred because of its low accuracy [4]. Surgery is the main diagnostic and therapeutic approach in case of a suspicious renal tumor. Although F-18 FDG PET/CT generally is an accurate diagnostic method for tumor definition in many malignancies, there are conflicting results in renal cell cancer with insufficient number of reports in this subject [5-8]. Especially there is lack of investigation of radiological borderline renal tumors by PET/CT as stated in a recent review by Khandani *et al.* [9]. We aimed to evaluate patients with prediagnosis of renal cell carcinoma who were referred for F-18 FDG PET/CT examination retrospectively in order to discriminate primary tumor by dual time imaging method.

## MATERIALS AND METHOD

### Patients

Seventeen patients (55.2 ± 9.9 years old; 7 F, 10 M) with prediagnosis of renal cell carcinoma were included into the study. After routine physical examination, abdominal ultrasonography, CT or MRI, the patients underwent dual phase F-18 FDG PET/CT examination for diagnostic purposes between November 2009 and February 2012. All of the patients underwent nephrectomy operation (9 partial, 8 total, 11 right, 6 left) in the two weeks period after the PET/CT imaging.

### Image Acquisition

PET/CT studies were carried out by an integrated PET/CT scanner which consisted of a full-ring HI-REZ LSO PET and a six-slice CT (Siemens Biograph 6; Siemens, Chi-

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cago, Illinois, USA). Patients were instructed to fast for at least 6 h before F-18 FDG injection.

Blood glucose levels were measured before the study and F-18 FDG injections were administered only when the blood glucose levels were below the 11.11 mmol/l. F-18 FDG was administered to the patients by venous line and the dose was calculated according to the body weight (approximately 370–555 MBq). The early and delayed scans were acquired 60 and 120 min after the injection of the F-18 FDG. Diuretics (10 mg intravenous furosemide) were injected 30 min before the early and delayed scan in order to limit the physiological activity in the renal collecting system. The patients were instructed to void before the scanning. Non-contrast enhanced CT was performed for attenuation correction with the following parameters: 50mAs, 140 kV, and 5-mm section thickness in craniocaudal direction (whole body in early scan and covering the kidney for delayed scan). PET images were acquired in three-dimensional mode, from the base of the skull to the mid thigh and in early phase six-to-seven bed positions of 3 min and each were acquired in caudocranial direction. In the late phase additional acquisition covering the kidney alone was acquired at the same position as the early scan, which consisted of 2 or 3 beds. The CT data were matched and fused with the PET data automatically.

### Image Interpretation

Two nuclear medicine physicians, who were blinded to the clinical, radiological and pathological results, retrospectively evaluated PET/CT data. Early and delayed images were visually interpreted in the axial, coronal, and sagittal planes additional to maximum intensity projection (MIP) images. The findings corresponding to a mass lesion in CT were classified as positive if there was obvious FDG uptake that had intensity greater than physiological accumulation of the renal parenchyma and was distinct from the physiological excretion of the radiopharmaceutical in the collecting system in early and delayed phase (SUVmax>3). Additionally mass lesion with FDG uptake in late phase without FDG accumulation in early phase was considered positive. Standardized uptake values (SUVs) were obtained after drawing a region of interest with a diameter of 1 cm on the consequent PET scan slices at the site of the renal lesion in early and delayed scan. The slice with the maximal FDG uptake was picked for measurement of maximum SUV (SUVmax). The SUVmax in the early phase (SUVmaxE) and the delayed phase (SUVmaxD) were calculated according to the following formula: SUV=cdc/(d/w), where cdc is the decay-corrected tracer tissue concentration (in Bq/g); d, the injected dose (in Bq); and w, the patient's body weight (in g). Furthermore, the retention index (RI) was calculated according to the equation of 100 x (SUVmaxD- SUVmaxE)/ (SUVmaxE). All PET/CT results were compared with the pathology results.

### Statistical Analysis

In order to compare numerical variables (SUVmax values) Mann Whitney U test and Paired Samples T test and to decide if the distribution of the variables is appropriate Kolmogorov Smirnov test were performed.

## RESULTS

Fifteen patients had malignant renal tumor (clear cell carcinoma in 13, papillary type in 1 and chromophobe type in 1 patient). Mean tumor size of the patients was 4±1,8 cm. During the mean 13±8.5 months follow up, 13 patients expe-

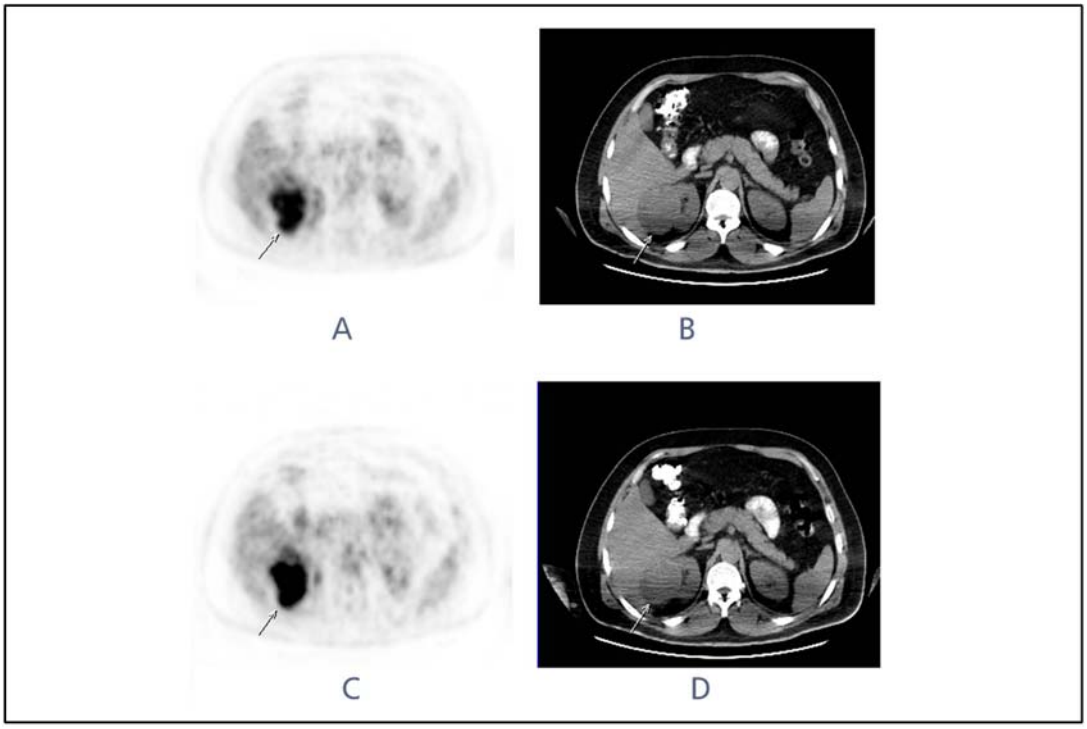


**Fig. (1).** (Patient No: 1 in the table) Early (**A**, **B**) and delayed (**C**, **D**) phase axial slices of PET and CT images. A mass lesion in the upper pole of right kidney with significantly increased FDG accumulation in both early and late phase revealed renal cell cancer in pathology results.

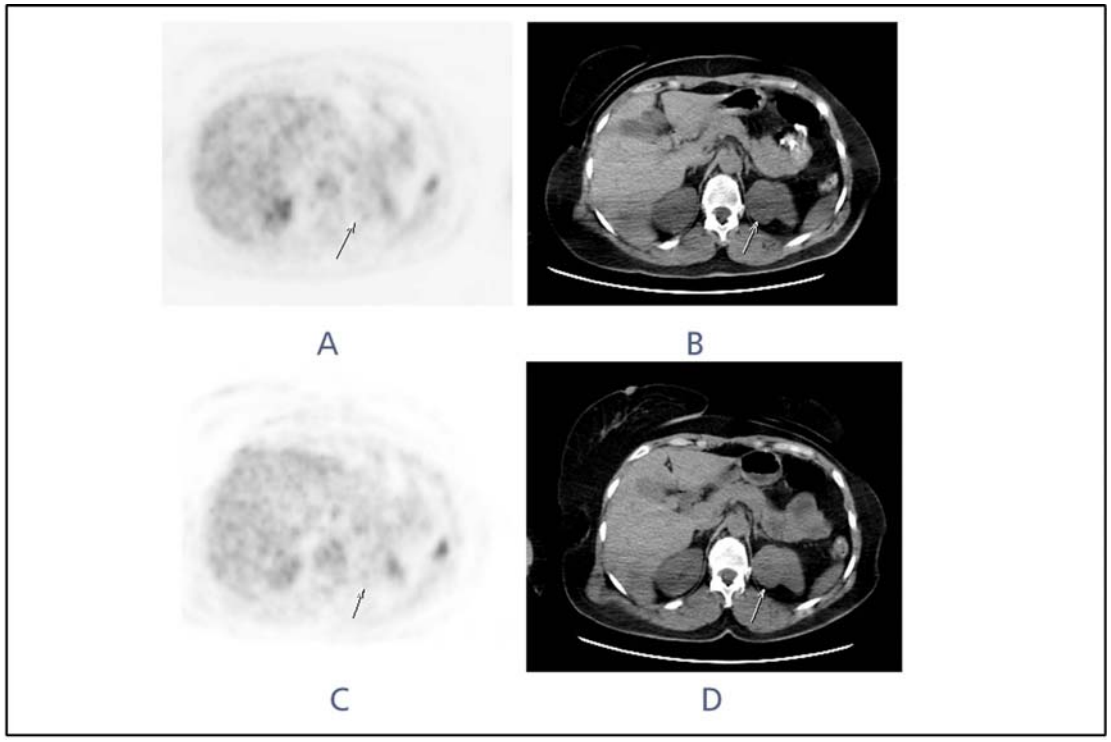


**Fig. (2).** (Patient No: 2 in the table) Early (**A**, **B**) and delayed (**C**, **D**) phase axial slices of PET and CT images. A renal lesion in upper pole of the left kidney without FDG accumulation in both phases was documented to be a renal cell cancer.

rienced disease free survival. One patient had one metastatic lymph node in 10th month control and 1 patient died because of another reason.

Two patients had non-malignant pathology of the kidney (oncocytoma in one and metanephritic adenoma in one patient). Both of the patients were interpreted as negative regarding renal cell cancer and SUVmax levels of the tumors did not rise in the late phase.

The interpretation of the PET/CT images revealed true positive results for 3 patients who showed increased activity accumulation in both phases (Fig. **1**; Patient No:1 in the table). However an increase in late phase was observed in only one patient, whereas SUVmax levels of the others decreased or stabilized in late phase (Fig. **2**; Patient No: 2 in the table). The TNM stages, Fuhrman grades of the patients and SUVmax levels of tumors in early and late phase and RI values as % percentages are summarized in (Table **1**).

The SUVmax values of the tumors were normally distributed according to the Kolmogorov Smirnov test and the difference between the early and delayed SUVmax values was not statistically significant according to Mann Whitney U test and Paired samples T test (p>0,05) (Fig. **3**).

According to early phase analysis the sensitivity, specificity, accuracy, positive and negative predictive value of PET/CT regarding diagnosis of primary tumor was 20%, 100%, 29%, 100% and 14%, respectively.

## DISCUSSION

In our patient population, we clearly demonstrated that F-18 FDG PET/CT is not beneficial in patients with prediagnosis of renal cell cancer because of extremely low sensitivity. Additionally late phase imaging warrants no further investigation in the patients with renal cell cancer. After this retrospective investigation we prefer not to continue early and late phase imaging in diagnosis of renal cell cancer because it does not indicate any diagnostic information.

Previous studies have concluded that FDG PET/CT might show distant metastases in even unexpected sites and it was an accurate modality in staging of the renal cell cancer [9]. Additionally another study has demonstrated that FDG PET may alter the treatment plan in 40% of the patients with renal cell carcinoma [10]. Renal cell tumors might spread to lung, lymph nodes, bone, liver and brain. Additionally adrenal metastases do occur in the renal cell cancer patients and F-18 FDG PET/CT can demonstrate all these metastatic sites [11]. There is also a previous study which has shown that the treatment response of advanced stage renal cell carcinoma might be achieved by F-18 FDG PET/CT which can also predict progression free survival and overall survival [12]. Khandani *et al.* have shown that primary tumors with low SUVbase levels respond better to neoadjuvant sorafenib [13].

Despite the diagnostic efficiency of PET/CT in staging, deciding response to treatment and tumor recurrence, the diagnosis of the primary tumor by PET/CT has not been evaluated sufficiently. Present data in the literature have demonstrated that F-18 FDG PET/CT might be inaccurate in the determination of the primary tumor. In contrast a previous study by Kumar *et al.* it has been reported that FDG PET might be employed in the diagnosis of the renal cell cancer depending on high SUVmax levels (7,9±4,9) of the renal malignant tumors in their study [14]. Unfortunately CT or MRI is not effective in discrimination of all of the tumors

**Table 1. TNM stage and Fuhrman grade of the patients and SUVmax levels of tumors in both phase and RI values.**

| Patient No | Age | Tumor Size | Type | TNM Stage | Fuhrman Grade | SUVmaxE | SUVmaxD | RI (%) |
|---|---|---|---|---|---|---|---|---|
| **1** | 48 | 8 cm | Papillary | T3aN0 | 1 | 9.3* | 13.5 | 45.3 |
| **2** | 52 | 4.5 cm | Chromofob | T1bN0 | 1 | 1.79 | 1.79 | -21.1 |
| **3** | 46 | 4.5 cm | Clear cell | T1bN0 | 2 | 2.21 | 2.15 | -2.7 |
| **4** | 54 | 3.7 cm | Clear cell | T1aN0 | 4 | 2.67 | 2.28 | -14.6 |
| **5** | 63 | 7.5 cm | Clear cell | T3aN0 | 2 | 3.83* | 3.62 | -5.4 |
| **6** | 47 | 1.5 cm | Clear cell | T1aN0 | 2 | 1.45 | 0.67 | -53.7 |
| **7** | 46 | 5.5 cm | Clear cell | T1bN0 | 3 | 4.2* | 3.75 | -10.7 |
| **8** | 76 | 3 cm | Oncocytoma | Benign | | 1.76 | 1.65 | -6.25 |
| **9** | 51 | 4 cm | Clear cell | T1aN0 | 1 | 1.85 | 1.62 | -11.9 |
| **10** | 38 | 3 cm | Clear cell | T1aN0 | 2 | 2.02 | 1.58 | -21.7 |
| **11** | 56 | 1.5 cm | Clear cell | T1aN0 | 2 | 2.94 | 2.41 | -18 |
| **12** | 55 | 5 cm | Clear cell | T3aN0 | 2 | 2.9 | 2.64 | -7.2 |
| **13** | 70 | 4.5 cm | Metanepfritic | Benign | | 2.69 | 2.3 | -7.8 |
| **14** | 58 | 3 cm | Clear cell | T3aN0 | 1 | 1.84 | 1.11 | -39.6 |
| **15** | 54 | 3 cm | Clear cell | T1aN0 | 1 | 2.31 | 2.22 | -39.9 |
| **16** | 55 | 5 cm | Clear cell | T1bN0 | 2 | 2.69 | 2.05 | -23.7 |
| **17** | 70 | 2 cm | Clear cell | T1aN0 | 2 | 2.24 | 2.15 | -4 |

* Indicates the high SUVmax values considered to be associated with positive (malign) lesions.

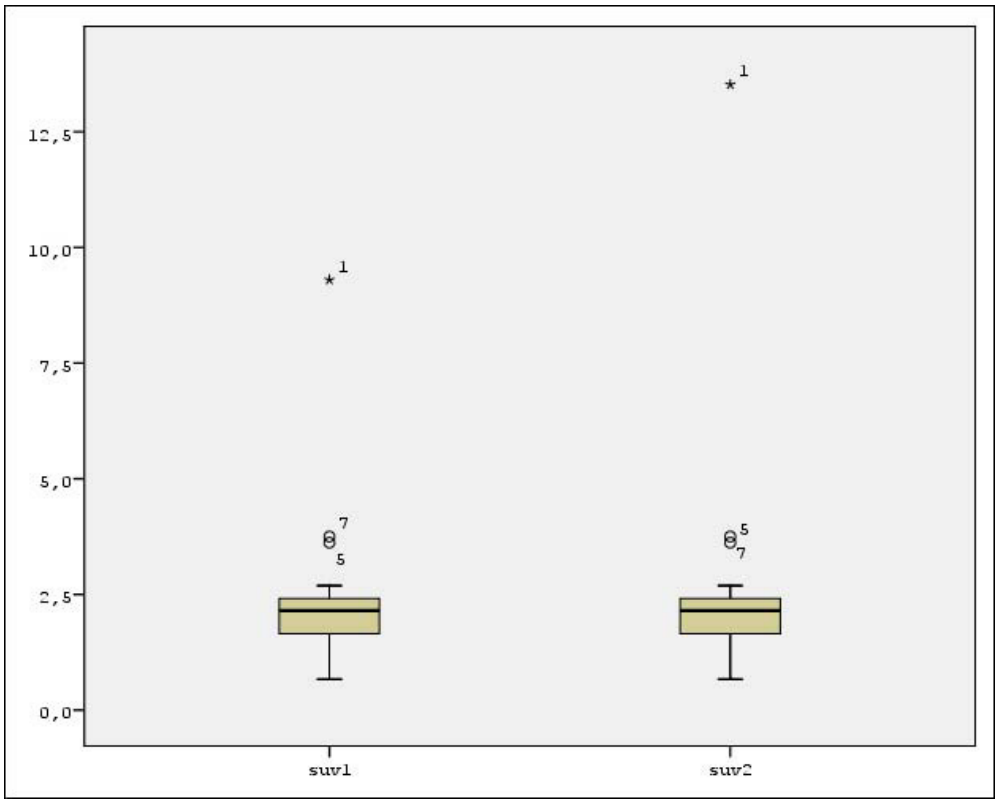


**Fig. (3).** Graphic demonstration of the SUVmax values of the tumors in the early phase (suv1) and the late phase (suv2).

and there are borderline tumors in respect to these imaging methods although MRI has been considered as an accurate method in the evaluation of indeterminate lesions [15]. This situation of renal cell cancer causes some unnecessary operations. In CT imaging the most important parameter is the degree of enhancement. Additionally the pattern of the enhancement, presence of calcification and tumor spreading patterns serve as helpful tools in the determination of subtype of renal cell cancer [16]. The definition of renal cell cancer depends on the enhancement degree which is above 25 HU as a cutoff value; however 10-25HU is considered as borderline tumors (indeterminate tumors) [3]. In our patient population the determination of indeterminate tumors couldn't be performed since in our retrospective analysis we couldn't provide sufficient contrast enhanced CT data. In our retrospective analysis of noncontrast CT portion of the PET/CT imaging we observed that all of the lesions had necrotic regions and none of the tumors involve other important imaging findings such as calcification.

The accuracy of F-18 FDG PET/CT was quite insufficient in our study population which predominantly consisted of renal cell cancer patients. Kang *et al.* reported sensitivity and specificity of the PET/CT 60% and 100%, respectively where CT revealed 92% and 100%, respectively [17]. These authors have concluded that low sensitivity limits diagnostic facility of PET/CT in renal cell cancer however regarding high specificity they have presented PET/CT as a problem solving tool. Also in our study the specificity was too high. Another comparative study has revealed sensitivity, specificity and accuracy of PET/CT ; 47%, 80% and 51%, respectively versus sensitivity and accuracy of 97% and 83% respectively in the CT [18]. In the same study although authors have demonstrated that PET/CT has no advantage over CT in the diagnosis of renal tumors, it might benefit in determination of distant metastasis of renal cell cancer. Ak *et al.* have revealed sensitivity, specificity and accuracy of 86%, 75% and 84%, respectively with coincidence PET and has reported another additional observation in their study that positive PET/CT may predict renal cell cancer although a negative study does not exclude it [7]. We also observed high (100%) PPV and extremely low NPV which supported suggestion of Ak *et al.* Ozulker *et al.* have performed a prospective study consisted of an important group of patients with 'indeterminate lesion' and reported sensitivity, specificity and accuracy as 47%, 66% and 50%, respectively for PET/CT [8]. They have also observed that Fuhrman grades of tumors with high SUVmax levels tend to be higher in their patient population [8]. However our findings do not support this idea as shown in (Table **1**). Kumar *et al.* have reported sensitivity of 85% in PET for characterization of the renal tumors and have claimed that tumor size was an important determinant in FDG accumulation of the tumor [13]. In our series there were two patients with 1.5 cm tumor size who were included in the false negative results thus our results support their suggestion. Additionally Kumar *et al.* have concluded that negative PET scan does not exclude malignancy especially in small or necrotic lesion. The significantly low sensitivity in our study might be a consequence of necrotic lesions which were present in almost all of our patients. Another theory about FDG accumulation of the renal cell cancer tissue is the correlation between GLUT-1 expressions although there are conflicting results about this subject [19, 20]. A review analysis has mentioned that possible reasons of non-FDG avid lesions might be related to the pathological type, differentiation degree and lesion size [21]. Another review about the role of PET/CT in genitourinary malignancies have indicated that for the diagnosis and staging of renal cell carcinoma, PET and CT might provide complementary information by high sensitivity of CT and high specificity of PET [22]. The specificity in our series was also high and since the CT has indicated malignancy, all of our patients underwent operation.

The limitations of our study are the retrospective structure of the study and homogenous distribution of our study group (mostly renal cell carcinoma). However this factor may also be an advantage of our study by providing more clear data about the PET/CT findings of renal cell carcinoma.

## CONCLUSION

Dual phase FDG PET imaging in the diagnosis of the renal cell cancer has been suggested as an efficient method by both a mouse model and previous studies in the human subjects [23, 18]. However in a homogenous group of patients with documented renal cell cancer patients our results have shown that FDG PET/CT is not an accurate method in the diagnosis of the renal cell cancer and dual phase imaging has no effect in the diagnosis thus this issue do not warrant any further investigation.

## CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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Declared none.

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