Small renal mass cryosurgery: Imaging and vascular changes

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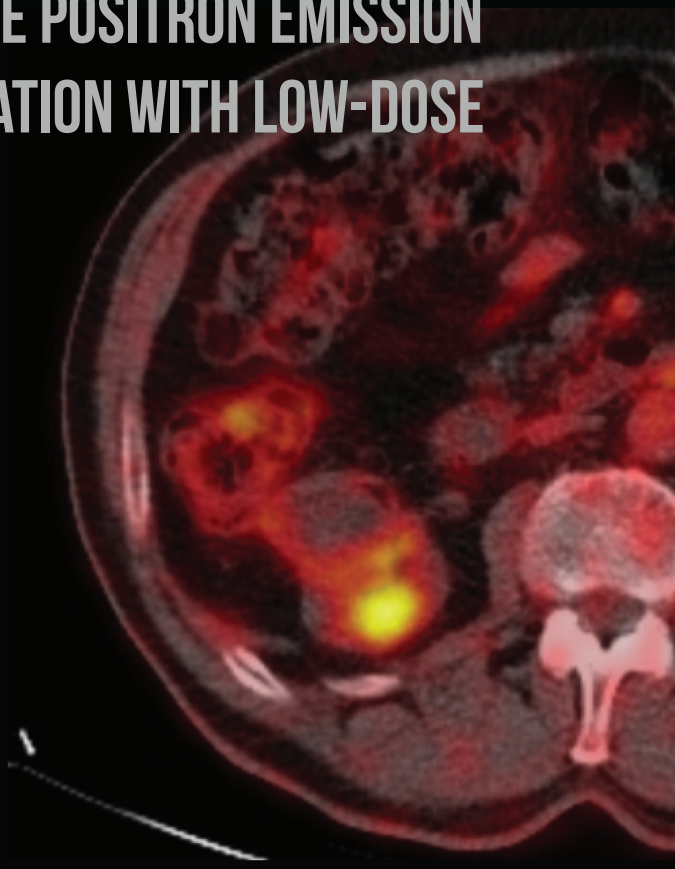
CHAPTER 7

INTERPRETATIONS OF ALTERNATIVE IMAGING METHODS FOR THE POST-CRYOSURGICAL RENAL MASS:

^{18}F- FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY IN COMBINATION WITH LOW-DOSE COMPUTED TOMOGRAPHY



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Abstract

Objectives

The success of cryosurgical treatment of small renal mass (SRM) is defined by the absence of contrast-enhancement at computed tomography (CT). The use of a contrast agent is relatively contra-indicated in patients with renal function impairment which mandates alternative follow-up strategies. The aim of this study is to describe the characteristics of molecular imaging with positron emission tomography (PET) in combination with low-dose CT in SRM treated with cryoablation (CA).

Materials and Methods

In selected patients set up for SRM cryoablation, several reasons were identified as criteria for performing PET-CT before and/or after cryoablation. Between July 2007 and January 2012, 9 patients (men:8, women:1; mean age 72 years) treated with cryosurgery and in case pre-operative work-up and/or follow-up with ^{18}F-FDG PET-CT were retrospectively studied.

Results

Patients were investigated at different times before and after ablation. The histology revealed renal cell carcinoma in 7 patients and oncocytoma in 2 patients. In 6 patients a PET-CT was performed before and after cryoablation. In one patient the PET-CT was performed before cryoablation and in 2 patients after cryoablation. Before cryoablation, there was clearly metabolic uptake of ^{18}F-FDG in the SRM in all patients. Following cryoablation, the absence of ^{18}F-FDG uptakes in the SRM could clearly be noticed. However, the tracer cannot always be distinguished from focal recurrence or reactive inflammatory tissue. In one patient, asymptomatic metastatic bone lesions were noticed performing PET-CT at follow-up.

Conclusions

This pilot study with ^{18}F-FDG PET-CT for the follow up of SRM cryosurgery showed that ^{18}F-FDG PET-CT imaging could be used to characterize cryoablative tissue injury at different times after CA. A longitudinal prospective study comparing ^{18}F-FDG PET-CT imaging to CT/MRI and histology is needed in order to establish its exact value in the follow-up of SRM cryoablation.

Introduction

The number of new renal cancer cases in the Netherlands was estimated to be 2000 in the year 2007 and is expected to increase to 2300 new cases by 2020. This increase may be due in part to an increase in the discovery of small incidental solid renal masses using cross-sectional imaging [1]. Recommended by principal guidelines nephron-sparing procedures for the management of small renal tumors have become the standard. Recently, cryoablation has been added as a viable treatment option for patients with small renal cell carcinomas (RCC) and those who are at high-surgical risk [2, 3]. It can be performed using image-guided percutaneous approaches or under direct visualization during laparoscopic (LCA) or open surgery. Image guided percutaneous cryoablation has potential advantages over surgical resection, including a decreased convalescence with reduced morbidity and appropriate oncological efficacy [4]. Patients who can particularly benefit from thermal ablation procedures are those who are poor surgical candidates because of compromised renal function and/or comorbid disease. However, patients with impaired renal function who are candidates for ablation can be poor subjects for the typical investigational methods used at follow-up.

According to principal guidelines, in practice, there is no consensus on which the set of diagnostic tools, time frame and frequency of follow-up of the cryoablated renal mass is recommended [2, 3]. Vascular damage and consequently ischemic injury is one of the mechanisms of action in cryoablation [5]. The mainstay of follow-up is the assessment of perfusion in and around the ablated area. Therefore, the current recommendation for follow-up of CA for small renal tumors is based on imaging of blood flow. The imaging method selected should be able to evaluate the presence or absence of vital tissue in the ablated area and measure the size of the lesion. Routinely, contrast-enhanced Computed Tomography (CT) or Magnetic Resonance (MR) imaging is used [6]. Intravenously administered contrast agents are used to identify contrast enhancement in the target lesion. The observation that the standard follow-up of cryoablated small renal masses in patients with declined renal function is not without risk of jeopardizing the remaining renal function led to the study of alternative methods of follow-up. The development of contrast-induced nephropathy is a significant complication of intravascular contrast medium use that is related to excess morbidity and mortality [7, 8]. The most important risk factor is pre-existing renal impairment which increases the risk for contrast-induced nephropathy by more than 20 times [9]. Therefore, alternative imaging not requiring radiographic contrast medium should be considered if the alternate imaging adequately addresses the diagnostic questions.

Alternative methods of imaging can focus either on the vascular or the molecular changes in the cryoablated zone. A method for studying the

molecular status of renal masses is the positron emission tomography (PET) in combination with low-dose CT, which assesses both renal mass anatomy and metabolic activity. Fluorodeoxyglucose (^{18}F-FDG) is the most frequently used radiopharmaceutical tracer in PET-CT imaging. However, it is not very accurate in distinguishing RCC from benign solid renal neoplasm. Relative differentiated cancers such as RCC show faintly or no ^{18}F-FDG uptakes that consequently result in negative PET-CT scans. As a result, it is not routinely used in the initial diagnostic work up of solid renal mass [10]. It does appear to be moderately useful in the detection of distant metastatic disease of RCC. There are nuclear tracers that better distinguish for RCC, but the availability is limited by their short half-life [11]. For example, carbonic anhydrase IX (CAIX), a transmembrane enzyme, plays a role in the tumor adaption to hypoxic conditions by regulating the pH of the intracellular and extracellular compartment. It is over-expressed in >95% of the clear cell subtype of RCC and is rarely expressed in the other known subtypes [12]. However, ^{18}F-FDG PET-CT can possibly be a reasonable alternative to the routine mode of imaging in those patients with relative or imperative contra-indications for the use of contrast-agents used in CT or MR imaging. This factor makes ^{18}F-FDG PET-CT of interest for the follow-up of cryoablated tumors. The hypothesis of this study was that if ^{18}F-FDG metabolisms could be detected in renal mass before cryoablation, it should not be detectable in the target zone after cryoablation.

The purpose of this study is to describe the spectrum of pre- and post-ablation ^{18}F-FDG PET-CT findings and define their value during follow-up for renal tumors treated with cryosurgery.

Materials and methods

All patients were identified with a solid renal mass suspected for malignancy. According to guidelines, patients were informed about optional treatment techniques and each typical follow-up method. All patients consented with CA. The same surgeon performed all laparoscopic or percutaneously CT-guided procedures. For cryoablation, multiple 17-gauge cryoprobes (Galil Medical, Yokneam, Israel) were used. Histological biopsies were obtained before cryoablation or intraoperatively.

Several reasons were identified as inclusion criteria to prefer PET-CT instead of CT or MR imaging: renal function impairment, contrast allergy, contra-indication for use of intravenous contrast medium, claustrophobia, metal implants, PET-CT already performed in a referring center, staging renal cancer, and the identification of a viable tissue metabolism in case of suspected local recurrence of renal cancer after initial ablative treatment.

Those patients that underwent ^{18}F-FDG PET-CT before and/or after renal mass cryoablation were retrospectively studied. Patients were identified in our institutional database. The local internal review board approved this study and its submission for publication.

PET-CT technique

^{18}F-FDG is a glucose analog with a positron-emitting radioactive isotope fluorine-18 substituted for the hydroxyl group at the 2nd position in the glucose molecule. PET imaging of tumors with the FDG-tracer is based on the observation that the tumor cells have an enhanced rate of glycolysis compared to most normal tissue. The uptake of glucose and analog FDG into malignant cells is facilitated by the increased expression of glucose transporter molecules at the tumor cell surface [13]. After intracellular transport, FDG is phosphorylated by hexokinase to FDG-6-phosphate, does not proceed further in the metabolic pathway and remains trapped in cells. PET identifies this selective focal accumulation of positron emitting FDG in malignant tumors. The glucose metabolic status can be analyzed quantitatively as the differential uptake ratio and distribution absorption ratio known as the Standardized Uptake Value (SUV) index.

Patients with renal function impairment (GFR-MDRD <60 ml/min/1.73m^2) before LCA treatment were offered ^{18}F-FDG PET-CT imaging. In case the target lesion showed metabolic activity before cryoablation, the PET-CT was repeated after LCA in order to assess therapy success. Post-cryoablation PET-CT imaging was performed within a minimum of three months after surgery. It was postulated that shortly following ablation within and around the ablation zone metabolic activity was to be expected at ^{18}F-FDG PET-CT. This would make it difficult to discriminate between inflammatory/reactive tissue and viable tumor tissue.

According to the local protocol, the treatment success of cryoablation is determined the first time postoperative contrast CT-imaging is performed within a minimum of 2 weeks after surgery and is defined by the absence of (focal) enhancement within the ablated tumor area [14]. However, under the circumstances of case-specific indications and awareness of preoperative PET-CT findings, a postoperative contrast CT or MR-imaging was not performed in all cases. In several cases, the PET-CT was combined with abdominal ultrasonography. A contrast-CT was only performed in those cases where PET-CT and or ultrasonography showed evidence for recurrence or metastatic disease.

Blood glucose level was measured prior to administrating FDG. The plasma glucose level was used to correct SUV measurements. A bolus of ^{18}F-FDG (range 141 - 233 MBq) was intravenously administrated 60-90 minutes prior to imaging. A PET-scan was performed from the skull base to the groin and

combined with a low-dose CT for attenuation correction and anatomic correlation. At preoperative PET-CT imaging, the metabolic uptake (SUV) was measured in the centre of the tumor and the liver for reference. At postoperative PET-CT, the metabolic uptake was calculated in the tumor center, the peripheral rim of the tumor, suspect lesions, and the liver for reference.

Results

General results

Between July 2007 and January 2012, a total of nine patients (mean age of 72 years) with small renal tumors treated with cryosurgery were retrospectively studied in case pre-operative work up and/or follow-up consisted of an ^{18}F-FDG PET-CT. Patient characteristics and general surgical information of this study are demonstrated in *table 1*. The median follow-up was 38 months (standard deviation ±12 months). Out of the 9 primary tumors that were treated with cryoablation, 7 were histological diagnosed as malignant and 2 as benign.

Indications for PET-CT before and or after LCA were: renal function impairment (n=6), suspicion for local recurrence following LCA (n=1), contraindication for intravenous contrast medium use (n=1), and in one patient a PET-CT was performed at the referring centre for staging purposes.

Table 1.

Patient characteristics and demographics. CA=cryoablation; RCC=renal cell carcinoma; GFR-MDRD=Glomerular Filtration Rate – Modification of Diet in Renal Disease.

Study number	Age at time CA (years)	Gender	Tumor size (mm)	Histology	GFR-MDRD	Solitary kidney
1	76	M	45	clear cell RCC	31	no
2	80	M	44	clear cell RCC	32	yes
3	72	M	19	clear cell RCC	55	yes
4	68	M	36	clear cell RCC	61	no
5	64	F	30	chromophobe RCC	52	yes
6	79	M	40	clear cell RCC	65	no
7	64	M	43	clear cell RCC	33	no
8	70	M	38	oncocytoma	99	no
9	75	M	48	oncocytoma	21	no

During follow-up of the 7 patients that were diagnosed with RCC, one patient was diagnosed with metastatic disease, one patient was diagnosed with a focal recurrence of RCC in the ablated area, and in one case a metachronous renal tumor was diagnosed in the previously treated solitary kidney.

Retrospectively, the SUV scores were calculated in the liver, the centre of the renal tumor and the surrounding rim of the ablation zone. Before cryoablation, there was clearly metabolic uptake of ^{18}F-FDG in the renal tumor in all patients (n=8). In this series we performed a PET-CT before and after ablative surgery in 6 cases [*table 2*]. It was clearly noticed that metabolic uptake of ^{18}F-FDG can be detected in solid renal lesions and, therefore, this could be used as a reference to discriminate for metabolic activity after renal mass cryoablation. In all those cases we found a significant decrease of metabolic FDG-uptake in the centre of the cryoablated tumors. However, in the surrounding rim of the ablation area in some patients, clear absence of the ^{18}F-FDG tracer could not always be distinguished from focal recurrence or reactive inflammatory tissue.

Table 2.

In 6 patients ^{18}F-FDG PET-CT imaging was performed before and after cryoablation. SUV scores before CA (a), at first time follow up (b), and consecutive (c, d, e) follow up.

Patient number	SUV renal mass centre	SUV renal mass periphery	SUV liver
2a	1.8	1.7	2.6
2b	0.8	3.1	2.4
2c	0.7	3.1	2.6
3a	3.2	2.8	2.8
3b	3.2	2.6	3.2
4a	3.9	3.3	3.2
4b	1.5	2.2	3.0
4c	0.6	0.9	2.3
4d	0.6	0.9	2.7
4e	0.7	0.7	3.2
5a	1.95	1.95	2.95
5b	1.4	2.9	3.2
5c	1.4	2.1	3.0
7a	2.5	2.6	2.8
7b	1.5	2.7	3.2
7c	1.5	2.9	3.4
9a	3.1	3.5	3.7
9b	1.0-1.5	4.5-4.7	3.0

Case reports

The first patient (*number 1*) was diagnosed with a 45mm diameter renal mass in the left kidney at contrast-CT and referred for LCA. Histology revealed clear cell RCC. Because of the patient's declined renal function, PET-CT was offered as the method of imaging at initial follow-up. There was no baseline preoperative PET-CT scan performed for comparison. The follow-up PET-CT at 10 months showed no metabolic activity in the centre of the ablation zone. However, there was some uptake of FDG around the border of the initial tumor. This could be due to reactive, inflammation or rest tumor activity. This test was not conclusive in view of the absence of a baseline PET-CT. The patient did have consecutive PET-CT imaging at 2 and 3 years follow-up. Both scans reported no evidence of tumor activity in the ablation zone. The activity as noticed at the first post-cryo PET-CT was no longer visible. The low-dose CT scans showed a decrease in size of the ablated tumor. In this case, there were no contrast CT or MR scan performed as control study. At 67 months follow-up, no recurrence or the novo renal tumor was found using ultrasonography.

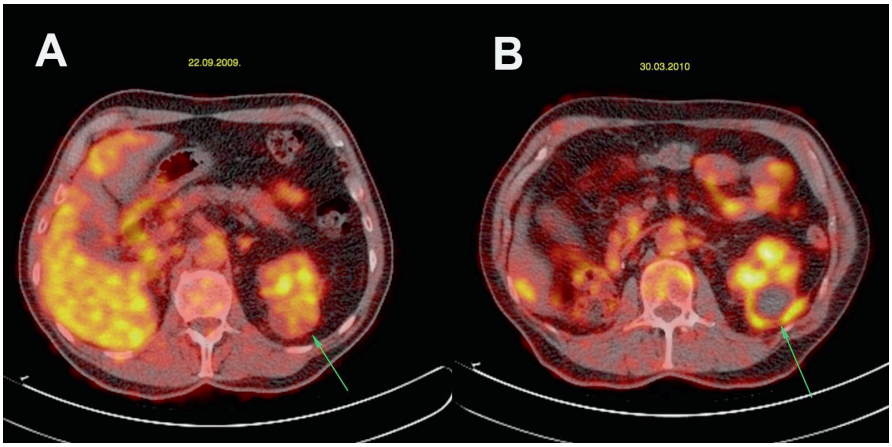
Patient number 2 was diagnosed with a 44mm diameter RCC of a solitary left kidney. Medical history revealed a right radical nephrectomy for RCC. The renal function impairment was the reason for a PET-CT scan prior to ablative surgery. Hypo-intense (compared to the liver) FDG-uptake (SUV 1.8) was noticed in the renal mass centre [*figure 1-A*]. Contrast-CT at one month after cryoablation showed a complete ablation of the tumor with some inflammatory reactive tissue in the perirenal fat. Five months post-cryoablation, the PET-CT image showed no metabolic activity in the ablation zone (SUV 0.8). However, some activity was noticed in the perirenal fat covering the outer border of the ablated tumor (SUV 3.1). This activity could be due to reaction or inflammation [*figure 1-B*]. A PET-CT scan, performed at 13 months follow-up, again showed no metabolic activity in the ablation zone (SUV 0.7) and again a slight FDG-uptake (SUV 3.1) was noticed in the perirenal fat covering the outer border of the ablated tumor. At 40 months follow-up, there was no sign of recurrence reported from the referring urological centre.

The medical history of *patient number 3* revealed a right radical nephrectomy for RCC and transurethral resection of single metachronous metastases in the bladder. Follow up contrast-CT scan showed an enhancing solid lesion of 19mm diameter in the left solitary kidney. Pre-cryoablation PET-CT showed iso-metabolic (compared to surrounding renal parenchyma) FDG-uptake in the lesion (SUV 3.2). During follow-up PET-CT, three months after LCA, there still was irregular FDG-uptake (SUV 3.2) noticed in the ablated tumor. However, the contrast-CT at 6 months after LCA showed a complete ablated tumor without contrast enhancement. No postoperative histological biopsy was performed in order to assess

recurrence. At one year follow-up the patient was diagnosed with metastatic prostate cancer without evidence for vital renal RCC at contrast CT.

Figure 1.

Patient 2: An example of ^{18}F-FDG-distribution in a renal mass before (A) and after 5 months cryoablation (B) at PET-CT. The light active iso-intense uptake in the tumor in the left kidney before cryoablation (green arrow panel A) has changed to a hypo-metabolic area after ablation (green arrow panel B). The activity around the ablated tumor in the perirenal fat is possibly due to inflammatory tissue reaction. A contrast CT-scan as control showed no enhancement of the ablation zone after treatment.



Patient number 4 was diagnosed with a 36mm diameter RCC of the left kidney. Because there was suspicion for macroglobulinemia (M. Waldeström), there was a contraindication for intravenous contrast medium usage. The pre-cryoablation PET-CT showed a moderate intense uptake of FDG (SUV 3.9) in the renal tumor [*figure 2-A*]. After LCA, the suspicion of macroglobulinemia was not proven and a control contrast CT was performed which showed a complete ablation of the tumor. Five months following LCA, the PET-CT revealed no FDG-uptake (SUV 1.5) in the ablated tumor as shown in *figure 2-B.* Also at 15 and 24 months follow-up the PET-CT scans showed no sign of recurrence [*figure 2-C and D*]. However, at 34 months follow-up, the PET-CT revealed FDG-uptake at the dorsolateral side of the left kidney in the perirenal fat that covered the ablation area [*figure 2-E*]. This uptake was considered suspect for RCC recurrence. And contrast-CT confirmed the diagnosis. However, the patient refused biopsy or retreatment. Contrast-CT at 40 months follow-up revealed the same enhancing tissue in the perirenal fat. However, no other suspected lesions and no enhancement

of the ablated zone was found. The suspected lesion did not increase in size. A repeat contrast-CT at 47 months follow-up this lesion has almost disappeared.

Patient number 5 had a right radical nephrectomy for RCC in the past. Now the patient was diagnosed with a suspected malignancy in the left solitary kidney. The pre-cryoablation PET-CT revealed a tumor with low FDG-uptake (SUV 1.95). Following cryoablation at 7 months, there was no accumulation of FDG in the ablated tumor (SUV 1.4). The border of the ablation site showed some metabolic activity that was not suspected to be focal recurrence. The consecutive PET-CT at 16 months follow-up again revealed no metabolic activity in the ablated tumor (SUV 1.4). Additionally, a renal ultrasound was performed. It showed a decrease in size of the ablated tumor (from 30 to 24 mm). However, there was suspicion of a new solid lesion superior from the ablation zone. At control contrast-CT, there was no enhancement of the ablated tumor. However, near to the abated tumor a new contrast-enhanced solid mass (21mm) was noticed [*figure 3-A*], conform the findings at ultrasound. It was considered a metachronous metastases and not evidence for focal recurrence after LCA. This tumor was almost completely endophytic and initially not recognized at follow-up PET-CT. The patient underwent a successful CT-guided percutaneous cryoablation for this second lesion. The histology confirmed RCC.

There was no PET-CT performed prior to LCA in *patient number 6*. A 40mm RCC was treated with LCA. The first follow-up CT at three weeks after surgery showed a complete ablation of the tumor at contrast-CT. However, the consecutive scan at 7 months showed new focal enhancement in the dorsal-central rim of the initially cryoablated tumor suspect for recurrence [*figure 4-X*]. At PET-CT, the centre part of the tumor showed no FDG-uptake (SUV 1.2-1.5) compared to the liver as reference (SUV 2.8). However, the dorsal-central area of the initial ablated tumor showed metabolic activity (SUV 2.7-2.8). This FDG-uptake could be related to an inflammatory reaction, focal recurrence or the accumulation of FDG in the collecting system [*figure 4-Y*]. The finding of the contrast-CT was decisive for offering consecutive treatment. This focal recurrence was successfully treated with CT-guided percutaneous cryoablation. Histological biopsy revealed recurrence of vital RCC tissue.

Figure 2.

Consecutive ^{18}F-FDG PET-CT imaging of a renal cancer before and after cryoablation. Green arrows indicate the tumor or the ablation site in the left kidney of patient number 4. Before surgery (A) there was metabolic activity noticed in the tumor. The low dose CT-scans showed consecutive decrease of the tumor volume and no metabolic activity was measured in the tumor using ^{18}F-FDG PET at 5 months (B), 15 months (C), and 24 months (D) follow-up after LCA. However, at 34 months new developed metabolic activity is noticed in the perirenal fat that covered the ablated tumor (green arrow panel E).

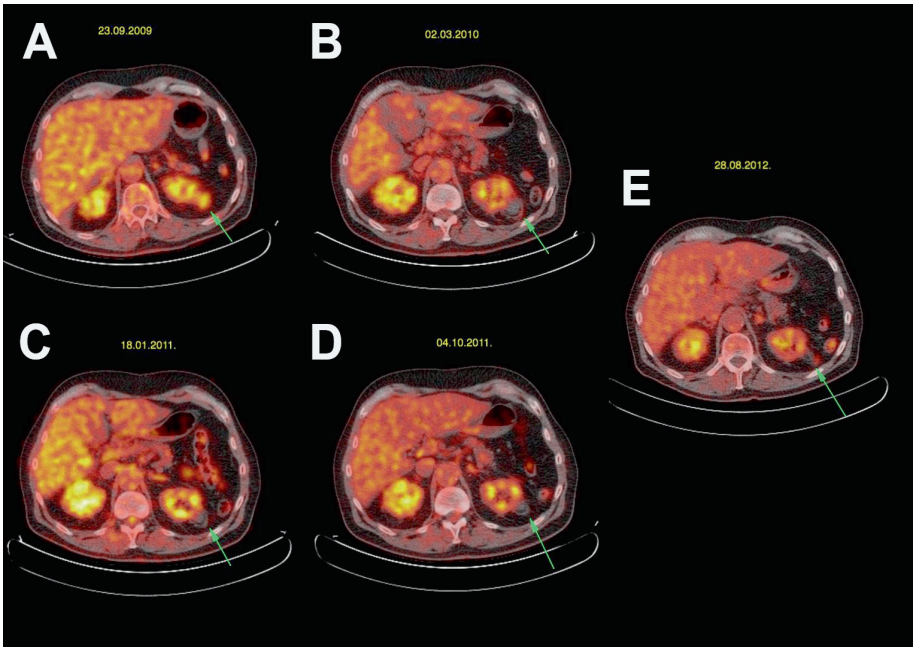
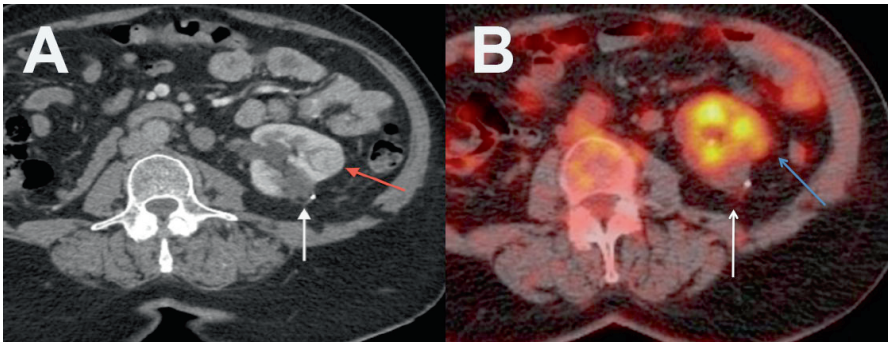


Figure 3.

Imaging at 15 months follow-up of patient 5. Panel A: Intravenous contrast-enhanced CT-scan in patient number 5 showing a non-enhancing zone (white arrow) at the side of the renal lesion treated with LCA. A second solid lesion with clear contrast-enhancement (red arrow) was noticed. Panel B: At ^{18}F-FDG PET-CT the ablation zone showed no metabolic FDG-uptake (white arrow). The blue arrow indicates the region of the metachronous RCC with FDG-uptake (SUV 3.1).



Patient 7 was offered a PET-CT because of poor renal function before treatment of a suspected renal lesion (43mm) on the upper pole of the right kidney. At the centre of this tumor a low FDG-uptake (SUV 2.5) was found at the pre-cryoablation PET-CT [*figure 5-A*]. The patient underwent LCA via a retroperitoneal approach. Histology revealed a clear cell carcinoma. At contrast-CT, performed 2 weeks following surgery, the tumor showed consistent enhancement of the superior-anterior part that was considered as an incomplete ablation with persistent vital tumor as a result. Consequently the LCA was repeated by intraperitoneal approach. The PET-CT at six months post-LCA showed the now two times cryoablated renal mass without clues for vital tumor tissue (SUV at the tumor centre was 1.5) [*figure 5-B*]. However, now there were two FDG avid bone localizations that were strongly suspected to be osteolytic metastases as is shown in *figure 6*. The contrast-CT as control and for further dissemination study showed no particular enhancement of the ablated tumor. The bone metastases were treated with external beam radiation. During follow-up pulmonary metastases were diagnosed and systemic treatment was administrated.

Figure 4.

At 8 months following LCA for patient 6, a focal contrast-enhanced area at the posterior side within the ablation zone was noticed on contrast CT-scan (X, blue arrow). Although not as sharply distinctive as the contrast CT-scan we noticed metabolic activation in the same posterior rim area at ^{18}F-FDG PET-CT-scan (Y, blue arrow).

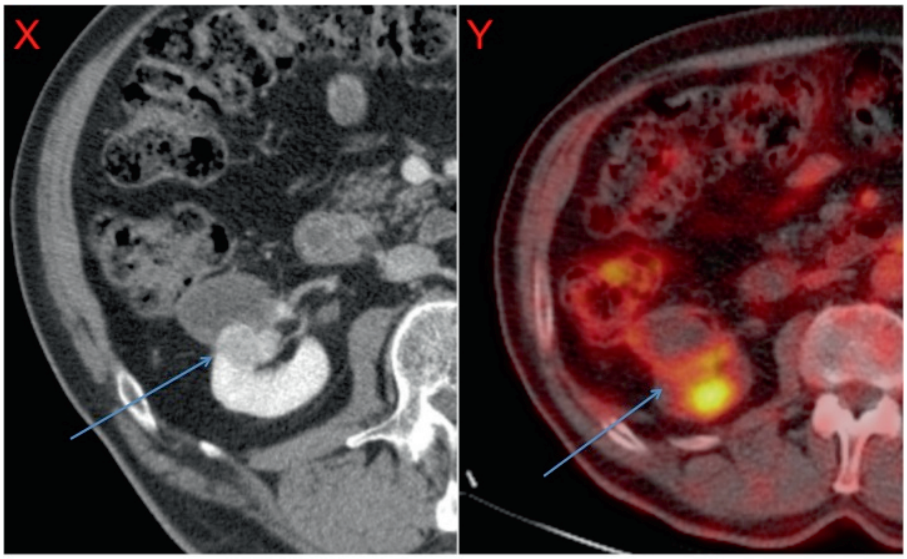


Figure 5.

Patient 7; Before treatment (A) the renal tumor in the right kidney shows a low FDG-uptake at ^{18}F-FDG PET-CT. The PET-CT scan after treatment (B) shows the same tumor without signs of the existence of vital tissue. Green arrows indicate the tumor before (A) and after (B) cryoablation.

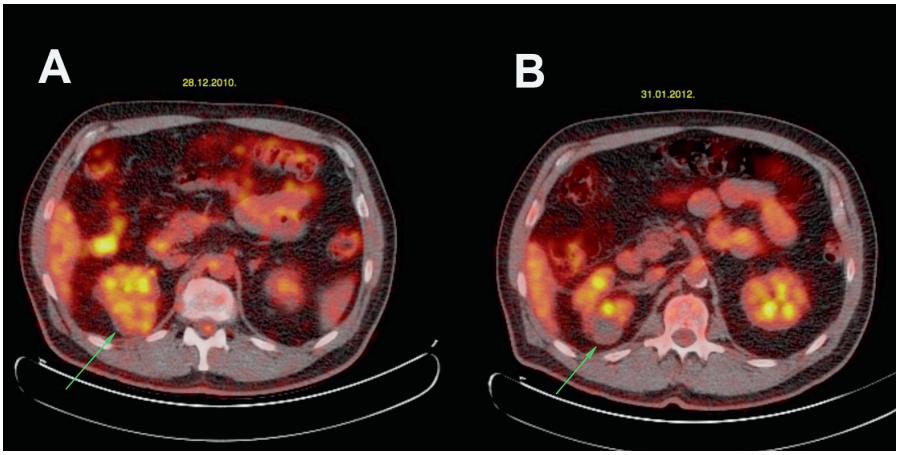
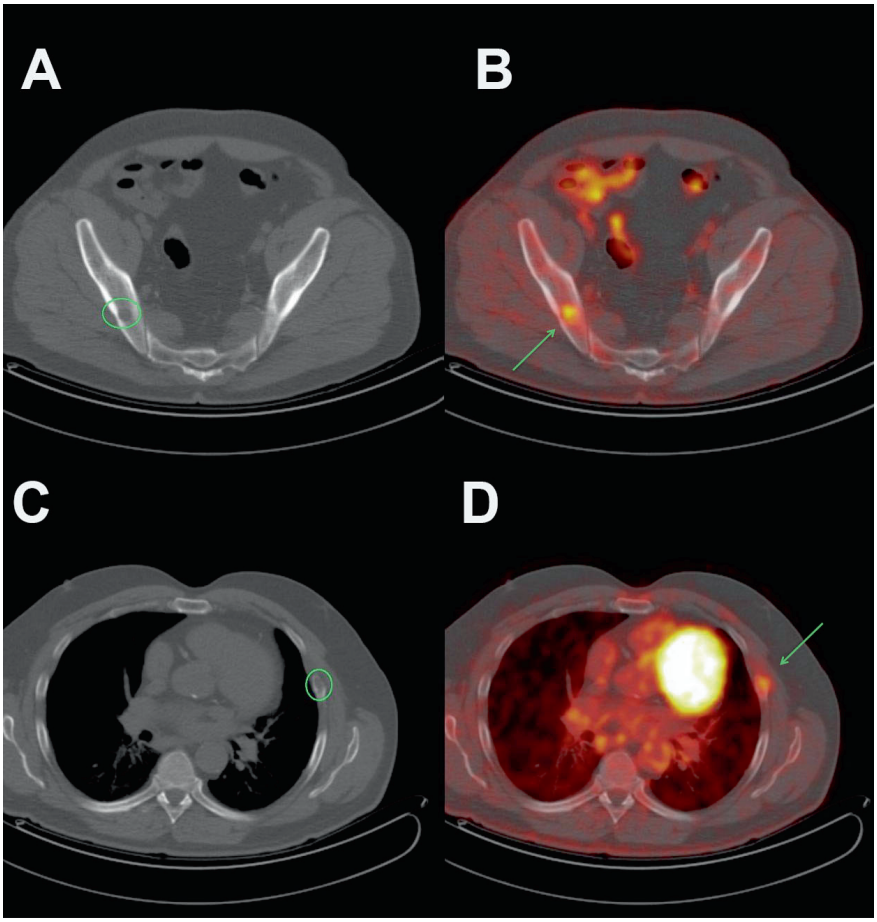


Figure 6.

Panel of ^{18}F-FDG PET-CT imaging at 6 months follow up of patient 7. There are two FDG avid bone localizations strongly suspected of being metastases (A, B). The low dose CT-scan without contrast shows cystic lesions in the right iliac bone (A, green circle) and in the 5th left costal rib (C, green circle). Both cystic locations correlated with the "hot spot" FDG-uptake as shown in B and D (green arrows).



Patient number 8 was referred for laparoscopic cryoablative treatment of an incidentally discovered solid renal mass in the left kidney. The referring centre performed an ^{18}F-FDG PET-CT for dissemination purposes. The PET-CT showed a metabolic active (SUV 5.7) tumor at the upper pole of the left kidney. The patient underwent LCA for the mass in the upper pole. The histology obtained by intraoperative biopsies revealed oncocytoma. Because of the benign nature of this renal mass, no postoperative PET-CT was performed. The post-operative contrast-CT showed a complete ablation of the renal mass.

Patient number 9 was diagnosed with a solid renal mass of 48 mm diameter in the left kidney. This patient was offered PET-CT prior to LCA because of poor renal function. In case of proven malignancy, we could offer follow-up using PET-CT. At pre-cryoablation PET-CT, there was FDG uptake (SUV 3.1) in the tumor located in the left kidney. Even though the intraoperative biopsies revealed a histological diagnosis of oncocytoma, the patient was offered a PET-CT to define treatment success. After cryoablation, in comparison with the PET-CT before cryoablation, there was a changed image of the tumor in the left kidney with a recognizable pattern of isometabolic to no metabolic activity (SUV 1.0-1.5). There was no contrast CT performed as control.

Discussion

In 2005, the first report of using fused PET-CT imaging for the follow-up of a renal mass treated with cryoablation was published [15]. This case report showed that a decrease of molecular activity was found using PET-CT in the renal lesion after cryosurgery compared to the PET-CT prior surgery. The purpose of the present study was to determine whether tracer uptakes found at baseline and no-tracer uptake at follow-up in ^{18}F-FDG PET/CT could be used to assess the response to cryoablation for RCC.

The patients reported in this study were in 8 out of the 9 cases referred for laparoscopic cryoablation after assessment of the diagnosis of a solid renal mass suspected to be malignant. In this series, we performed a PET-CT before ablative surgery in 7 cases. We noticed that solid tumors could be detected as metabolic active lesions at ^{18}F-FDG PET-CT imaging. The ^{18}F-FDG PET-CT is not routinely used in the initial diagnostic work up of solid renal masses [10]. Furthermore, it does not discriminate between benign and malignant renal growth. Hence, the present study showed metabolic activity in oncocytoma and RCC. The number of cases was too limited in order to be able to assess a possible difference in the SUV for benign and malignant renal masses. However, the present study showed that metabolic uptake of ^{18}F-FDG can be detected in solid renal lesions. Therefore, this could be used

as a reference to discriminate for metabolic activity after renal mass cryoablation. In all those cases, we found a significant decrease of metabolic FDG-uptake in the centre of the cryoablated tumors. Therefore, we postulate that ^{18}F-FDG PET-CT imaging can be used as an alternative-imaging method to contrast-CT/MR imaging for the assessment of treatment success of LCA.

In all cases, there was a relative or imperative reason for the use of an alternative imaging technique other than intravenous contrast medium imaging to assess the renal tumor viability before and after cryoablation. One of the major benefits of ^{18}F-FDG PET-CT is that there are no contraindications for patients with decreased renal function. The patient's height, body weight and medical history of diabetes mellitus are essential for the interpretation of SUV measurements [16]. FDG-PET and CT are imaging modalities that have been validated in routine clinical practice. Integrated PET/CT combines PET and CT in a single imaging device and allows morphological and functional imaging to be carried out in a single procedure. This integration has advantages for the assessment of the vitality of a small renal mass (SRM) before and after cryoablation. Vascular damage and consequently ischemic injury are a significant mechanism of action in CA [5]. The current mainstay of follow-up is the assessment of vascular flow in and around the ablated area. Therefore, the recommendations for follow-up of CA for a small renal tumor are based on imaging of blood flow [14]. However, identifying the absence of metabolic activity using PET can also assess the viability of tissue. Another morphologic feature is that cryoablated renal tumors tend to decrease in size over time. At three years follow-up of patients treated with LCA, Gill et al observed a gradual involution of the ablation zone diameter by an average of 75%. Furthermore, 38% of the ablation zones were undetectable on MR imaging after 3 years follow-up [17]. Even though low-dose non-contrast enhanced CT is not intended for radiological diagnosis, it makes it possible to see a decrease in size of most ablated tumors over time.

One of the limitations of this study was the resolution achieved by PET-CT. It does not allow for accurate interpretation of metabolic activity at the rim borders of the ablation zone. The measurement of SUV in an area selected smaller than 1 cm diameter becomes inaccurate and, therefore, selection of the region of interest is of the utmost importance. However, at a short distance, a focal recurrence can be surrounded by FDG concentrating morphologic structures as the normal renal parenchyma and/or the urinary collecting system. Artefacts as a result of high FDG concentration in the urine can be minimized by adequate pre-hydration. In patient number 6, FDG-accumulation was found in the rim of the ablation zone at the dorsal-central border. Initially this was not recognized as a suspect for focal recurrence. Contrast-enhanced CT showed focal enhancement and, therefore, the patient underwent consecutive biopsy and cryosurgery.

Histology confirmed the presence of viable RCC tissue. The post-LCA PET-CT of patient number 3 revealed irregular FDG accumulations in the ablation zone. However, contrast-CT three months later showed no evidence of enhancement in the ablated tumor. In this case, the limited tumor dimension (19mm diameter) possibly hampered the interpretation of the PET-CT findings.

After LCA, in four more patients, metabolic activity was noticed at the rim of the ablation assessed by ^{18}F-FDG PET-CT. In patient number 4, this was found in the peritumoral fat by the third consecutive PET-CT almost three years post-LCA, whereas previous scans showed no peripheral metabolic activity. Therefore, this must be considered a suspect for metastases. However, this is not confirmed by histology. In patient number 1, 2 and 5, the metabolic activity of the peripheral rim was encircling the metabolic inactive ablation zone as noticed in the first PET-CT following cryoablation. This seems comparable to the literature where findings by CT and MRI of rim enhancement were noticed around the ablation zone in 17-30% of cases at 1 month after treatment [18-20]. This peri-ablational enhancement is considered benign. It is suggested that this is a physiologic response to thermal injury, and it appears as a relatively concentric, symmetric, and uniform process with smooth inner margins [6]. It seems that during the first months after ablation this finding is of no consequence; however, if it were to occur later at follow-up it could be interpreted as a sign of recurrence and will typically appear as irregular peripheral enhancement. The PET-CT findings of patient number 4 can possibly be interpreted as such.

In this series, the PET-CT cross-sectional area stretched between the skull base and the groin. Therefore, using this technique, more than the local ablation site could be studied. The cross-sectional area of the thorax and abdomen, in combination with integrated method of imaging, enables us to locate metabolic active pulmonary, lymph node, or bone metastases. In patient number 7, two asymptomatic bone metastases were found this way. However, these lesions could also have been noticed during a cross sectional contrast-CT of this area.

The search for the best method to assess treatment success after cryosurgery for renal tumors remains subject to new investigations. However, in patients with relative or imperative contra-indications for the use of contrast-agents in CT or MRI imaging, ^{18}F-FDG PET-CT may be a reasonable alternative in the follow-up in CA of small renal masses. The total accumulated radiation dose of consecutive CT scans performed is considered negative related to the follow-up of LCA. The radiation dose with PET-CT is lower compared to the radiation dose of a full diagnostic cross-sectional CT scan. The radiation dose of 185 MBq ^{18}F-FDG is about 3-4 mSv.

To our knowledge, this pilot study is the first to assess ^{18}F-FDG PET-CT imaging reviewing the spectrum of pre- and post-ablation PET-CT findings and to discuss its value in follow-up of renal tumors treated with cryosurgery. However, this study has, as have most pilot studies, many limitations. Only a few patients, at different times after CA, were studied in order to examine the possibility of using ^{18}F-FDG PET-CT imaging to characterize the lesion. No longitudinal data were collected, and no direct comparison with CT/MRI was intended. Furthermore, the majority of PET-CT findings are not confirmed by histology. Therefore, the accuracy of PET-CT could not be assessed. However, the results of the present study show that ^{18}F-FDG PET-CT can be used in the follow-up in patients with small renal masses that underwent CA. We assume this justifies a larger prospective and comparative study in order to determine the exact value of this technique for assessing treatment success and detecting recurrent tumors after CA.

Conclusion

This experience with the ^{18}F-FDG PET-CT for the follow-up of renal mass CA showed that ^{18}F-FDG PET-CT imaging could be used to characterize cryoablative tissue injury at different times after CA. A longitudinal prospective study comparing ^{18}F-FDG PET-CT imaging to CT/MRI and confirmed by histology is needed in order to establish its exact value in the follow-up of renal mass CA.

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