

Clinical utility of ^{18}F -FDG PET/CT in staging and treatment planning of urachal adenocarcinoma

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Running Title: PET/CT in UrC-ADC

ABSTRACT

Purpose: Our objective was to evaluate the impact of utility of ¹⁸Fluorine (¹⁸F)-Fluorodeoxyglucose (FDG) positron emission tomography (PET) computed tomography (CT) in the management of urachal adenocarcinoma (UrC-ADC).

Methods: A retrospective analysis of patients with UrC-ADC from 2001-2019 at Memorial Sloan Kettering was performed. Mayo stage prior to ¹⁸F-FDG-PET/CT, rates of detection of the primary malignancy and metastases on ¹⁸F-FDG PET/CT, Mayo stage after ¹⁸F-FDG-PET/CT, and changes in patient management were determined.

Results: Of 21 patients with UrC-ADC prior to ¹⁸F-FDG-PET/CT, Mayo staging was I/II in 8, III in 3 and IV in 10. ¹⁸F-FDG-PET/CT detected previously unidentified metastases in 8 of 21 (38%) patients, resulting in upstaging of disease in 3 (14%) patients, and a change in treatment in 4 patients (19%).

Conclusion: ¹⁸F-FDG PET/CT has clinical utility in patients with UrC-ADC by identifying metastatic disease not appreciated on anatomic imaging, leading to changes in staging and patient management.

Key words: Urachus, urachal adenocarcinoma, ¹⁸F-FDG PET/CT, staging

INTRODUCTION

Urachal adenocarcinoma (UrC-ADC) is an aggressive non-urothelial tumor of the urachus, a remnant of the embryological structure connecting the allantois and fetal bladder. (1–4) 20-50% of UrC-ADC patients present with metastatic disease. (5–7) The stage of UrC-ADC is the most important prognostic factor, with 5-year survival rates of 63%, 55%, 19%, and 8% for stage I, II, III, and IV, respectively. (2, 6) Accurate and effective staging is therefore critical in the assessment of UrC-ADC and guiding treatment. (3, 5, 8, 9)

While FDG PET/CT has demonstrated value in many malignancies (10–12), UrC-ADC are often mucinous in histology (1–4), and mucinous malignancies may demonstrate low or absent ^{18}F -FDG uptake. (13) Thus, ^{18}F -FDG PET/CT may not be a sensitive for UrC-ADC. Data for FDG PET/CT in UrC-ADC is limited to brief reports and pictorial essays. (14–17) The objective of this study was to determine if ^{18}F -FDG-PET/CT impacts systemic staging of UrC-ADC and its clinical management.

MATERIALS AND METHODS

Study Design

This HIPAA-compliant, retrospective, single-institution study was performed under Institutional Review Board approval with the requirement to obtain informed consent waived by the board. Our Hospital Information System was screened for patients with pathologically proven cases of UrC-ADC diagnosed between January 2001 and January 2019 who underwent imaging with contrast-enhanced CT or MRI and ^{18}F -FDG PET/CT within 6 weeks and prior to systemic or radiation therapy. Patients with the following characteristics were excluded: incomplete clinical or histopathological records, prior malignancy, non-adenocarcinoma histology of UrC, no ^{18}F -FDG-PET/CT imaging, no conventional CT or MR imaging within 6 weeks prior to the ^{18}F -FDG-PET/CT, chemotherapy or radiation therapy prior to ^{18}F -FDG PET/CT. For patients included in our analysis,

medical records were reviewed to determine age, gender, and pathologic subtype (mucinous or non-mucinous) of the tumor.

Determination of Stage Prior to ^{18}F -FDG-PET/CT

The Mayo staging system for UrC (**Table 1**) was used to classify the urachal tumors. [5] Contrast enhanced CT (or MR for one patient) was utilized to determine an imaging stage prior to ^{18}F -FDG PET/ CT.

^{18}F -FDG-PET/CT Imaging and Interpretation

^{18}F -FDG-PET/CT and contrast-enhanced cross-sectional imaging studies were evaluated by a nuclear radiologist dual board certified in Nuclear Medicine and Diagnostic Radiology with 15 years of PET/CT experience (GAU) blinded to pre-PET/CT stage, assisted by a nuclear medicine fellow (JPD). SUVs, normalized to body weight, were determined on General Electric *AW* suite. According to standard ^{18}F -FDG PET/CT reporting, uptake was considered abnormal when it was focal, not considered physiologic or inflammatory, and with intensity greater than local background.

Determination of Stage Following ^{18}F -FDG-PET/CT and rate of upstaging

Metastases identified by ^{18}F -FDG-PET/CT that had not been detected in prior conventional cross-sectional imaging studies were recorded. ^{18}F -FDG PET/CT results were used to determine the patient's stage following ^{18}F -FDG PET/CT. Initial clinical stage was compared to clinical stage following ^{18}F -FDG PET/CT to determine the rate of upstaging. Changes in patient management based on ^{18}F -FDG PET/CT were recorded as determined from medical records. The ^{18}F -FDG-PET/CT scan results were confirmed with the histological data when available. When the histology was not available, imaging follow-up was utilized.

Characterization of primary malignancies

CT/MR images were reviewed to classify the primary UrC-ADC as well/ill-defined, solid/cystic, enhancing/non-enhancing, and for presence of calcifications. On FDG PET/CT, the primary UrC-ADC was classified as FDG-avid (above local background), and if avid, record SUV_{max} .

RESULTS

Patient Demographics

A Standards for Reporting of Diagnostic Accuracy Studies (STARD) diagram of patients screened and included in our analysis is presented in **Figure 1**. Demographics of the 21 patients included in the cohort are outlined in **Table 2**.

Mayo stage prior to ^{18}F -FDG-PET/CT

Before ^{18}F -FDG-PET/CT, Mayo staging was I/II in 8 (38%), III in 3 (14%) and IV in 10 (48%) patients. All metastatic disease detected on conventional cross-sectional imaging was histopathologically proven from at least one site. The most common sites of distant metastases were the peritoneum (n=6), lung (n=4), distant nodal (n=2), liver (n=2), pancreas (n=1) and soft tissue (n=1). Five patients had more than one site of metastatic disease.

Additional metastases detected by ^{18}F -FDG PET/CT

21 patients underwent ^{18}F -FDG PET/CT within 6 weeks of conventional imaging (**Table 3**), and prior to systemic or radiation therapy. In 11 patients, ^{18}F -FDG-PET/CT was performed prior to resection of the primary

malignancy, while in 10 patients ^{18}F -FDG-PET/CT was performed following resection of the primary malignancy. The median number of days from prior cross-sectional imaging to ^{18}F -FDG PET/CT was 17.3 days (range 0-42).

Previously undetected metastases were identified on ^{18}F -FDG PET/CT in 8 of 21 patients (38%). These included osseous metastases in 4 patients, nodal metastases in 3 patients (pelvic n=2, thoracic n=1), pancreatic metastases in 2 patients, and hepatic metastases in 1 patient. Two patients had more than one site of newly detected metastatic disease; osseous and nodal in one patient, osseous and pancreatic in another patient. The SUV_{max} of FDG-avid metastases ranged from 3.0-14.5. Histopathological confirmation was obtained in 3 patients (pelvic nodal and pancreatic in one patient, liver, pancreatic in the two other respective patients), while in 5 patients newly-detected metastases demonstrated increased size and/or FDG-avidity on subsequent imaging studies. Three patients (14%) were upstaged by FDG-PET/CT; Two patients were upstaged from Mayo stage II to IV and one patient was upstaged from Mayo stage III to IV.

Based on the findings on FDG-PET/CT, changes in treatment or escalation of therapy was undertaken in 4 of 21 patients (19%). An FDG avid pancreatic metastasis detected in one patient (previously considered a candidate for potentially curative surgical resection of the primary UrC-ADC) resulted in a systemic treatment with chemotherapy instead of surgery. An FDG-avid liver metastasis was detected in one patient (**Figure 2**) resulting in the initiation of systemic chemotherapy. In a third patient, FDG-avid pancreatic and osseous metastases led to treatment escalation with chemotherapy and radiation to osseous metastases. (**Figure 3**) A fourth patient (considered Mayo stage IV by CT and thus not upstaged by ^{18}F -FDG-PET/CT) being treated with chemotherapy alone was subsequently treated with radiation following detection of additional osseous metastases on ^{18}F -FDG-PET/CT.

Characteristics of primary UrC-ADC tumors on CECT and ^{18}F -FDG PET/CT

The characteristics of the primary tumors are discussed in an online supplement.

DISCUSSION

We evaluated the clinical utility of ^{18}F -FDG-PET/CT in staging of UrC-ADC. We found that ^{18}F -FDG-PET/CT detected additional metastases in nearly 40% and upstaged disease by radiographic criteria in almost 15% of UrC-ADC patients compared to cross-sectional imaging performed within 6 weeks prior. In addition, we found that ^{18}F -FDG-PET/CT resulted in a change in management or treatment plan in almost 20% of patients with UrC-ADC.

Because of the rarity of this tumor, the literature pertaining to ^{18}F -FDG PET/CT evaluation of urachal pathology consists primarily of case reports and smaller case series. The positive predictive value of imaging to detect malignancy pre-operatively is low when dealing with a urachal mass (18) as both benign and malignant urachal pathology can appear similar on CECT and ^{18}F -FDG PET/CT. (19, 20) Variable FDG avidity of UrC-ADC has been described in the literature to date. (21, 22) Guimaraes et al. described a primary UrC-ADC demonstrating increased FDG-uptake (without distant metastases) where ^{18}F -FDG PET/CT provided valuable information in diagnosis and initial staging of disease. (22) Zemen et al. described a false negative ^{18}F -FDG PET/CT finding in a mucinous urachal adenocarcinoma showing background FDG-uptake without evidence of metastatic disease. (23) Interestingly, Li et al. described ^{18}F -FDG PET/CT findings in a patient with a primary mucinous UrC-ADC showing low-level FDG avidity (SUV 2.4), with FDG-avid nodal and osseous metastases (SUV 6.9) (21) We noted a similar finding in our series of patients. Of the 4 patients with FDG-avid metastases and an evaluable mucinous primary UrC-ADC, the primary tumour was non-avid in one case.

Mucinous tumors have been shown to demonstrate low or background FDG uptake due to hypocellularity, potentially limiting the sensitivity of ^{18}F -FDG PET/CT. (13, 24) Mucinous tumor subtype comprised the majority (67%) of our patients with UrC-ADC (please see online supplemental methods and results). Half of these patients (7/14) developed FDG-avid metastatic disease.

We are limited by both the small sample size and the retrospective nature of the study design. In addition, the absence of data or guidelines for the use of ^{18}F -FDG PET/CT in UrC-ADC may have introduced

selection bias in our single-center analysis. However, due to the rarity of UrC-ADC, high-powered prospective studies would be difficult to undertake.

CONCLUSION

Our data suggests ^{18}F -FDG PET/CT has clinical utility in patients with UrC-ADC by identifying metastatic disease not appreciated on anatomic imaging, leading to changes in staging and patient management.

KEY POINTS

Question: Does FDG PET/CT impact the staging and management of urachal adenocarcinoma (UrC-ADC)?

Pertinent Findings: This retrospective analysis of 21 patients with UrC-ADC prior to chemo- and/or radiation therapy demonstrated that FDG PET/CT performed within 6 weeks of conventional CT/MR detected previously unidentified metastases in 8 (38%) patients, resulted in upstaging of disease in 3 (14%) patients, and a change in treatment management in 4 (19%) patients.

Implications for Patient Care: ^{18}F -FDG PET/CT has clinical utility in patients with UrC-ADC by identifying metastatic disease not appreciated on anatomic imaging, leading to changes in staging and patient management.

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Stage **Mayo classification [5]**

- 1 Confined to urachus/bladder
- 2 Beyond muscular layer of the urachus/bladder
- 3 Involving regional lymph nodes
- 4 Involving non-regional lymph nodes/ distant metastases

Table 1. Mayo classification staging system for urachal cancer

UrC-ADC patients		(n=21)
Age (years)	52.7 (range 32-75)	
Gender		
Female	8	
Male	13	
Histopathology		
Mucinous	14	
Non-mucinous	7	
Mayo stage (prior to FDG PET/CT)		
I/II	8	
III	3	
IV	10	

Table 2. Patient demographics for our cohort of 21 patients with UrC-ADC

Patient no.	Mayo stage prior to PET/CT	Prior cross-sectional imaging modality	Days from cross-sectional imaging to PET/CT	New metastases detected by PET/CT?	Sites of detected metastases, SUVmax	Change in stage following PET/CT?	Change in treatment following PET/CT?
1	IV	CT	3	Yes	Nodes (pelvic), 3.0	No	No
2	III	CT	38	Yes	Hepatic, 9.0	Yes (III to IV)	Systemic chemotherapy commenced
3	II	CT	40	No	No	No	No
4	II	CT	27	No	No	No	No
5	II	CT	3	No	No	No	No
6	IV	CT	36	Yes	Osseous, 12-14.5	No	Radiation commenced
7	IV	CT	0	Yes	Osseous, 4.2	No	No
8	III	CT	16	No	No	No	No
9	IV	CT	0	Yes	Osseous, 7.0; Nodes (thoracic), 3.0	No	No
10	II	CT	32	No	No	No	No
11	II	CT	26	No	No	No	No
12	IV	CT	4	No	No	No	No
13	IV	CT	7	Yes	Nodes (pelvic), 4.2	No	No
14	II	CT	42	Yes	Pancreatic, 4.0	Yes (II to IV)	Systemic chemotherapy commenced, no longer a candidate for curative surgery
15	IV	CT	0	No	No	No	No
16	IV	CT	2	No	No	No	No
17	IV	CT	7	No	No	No	No
18	IV	CT	16	No	No	No	No
19	II	CT	20	No	No	No	No
20	II	CT	40	Yes	Osseous, 5.0-6.8; Pancreatic, 7.3	Yes (II to IV)	Systemic chemotherapy and radiation commenced
21	III	CT & MRI	5	No	No	No	No

Table 3. Results of 21 patients with Urachal adenocarcinoma (UrC-ADC) undergoing ¹⁸F-FDG PET/CT following conventional CT or MR.

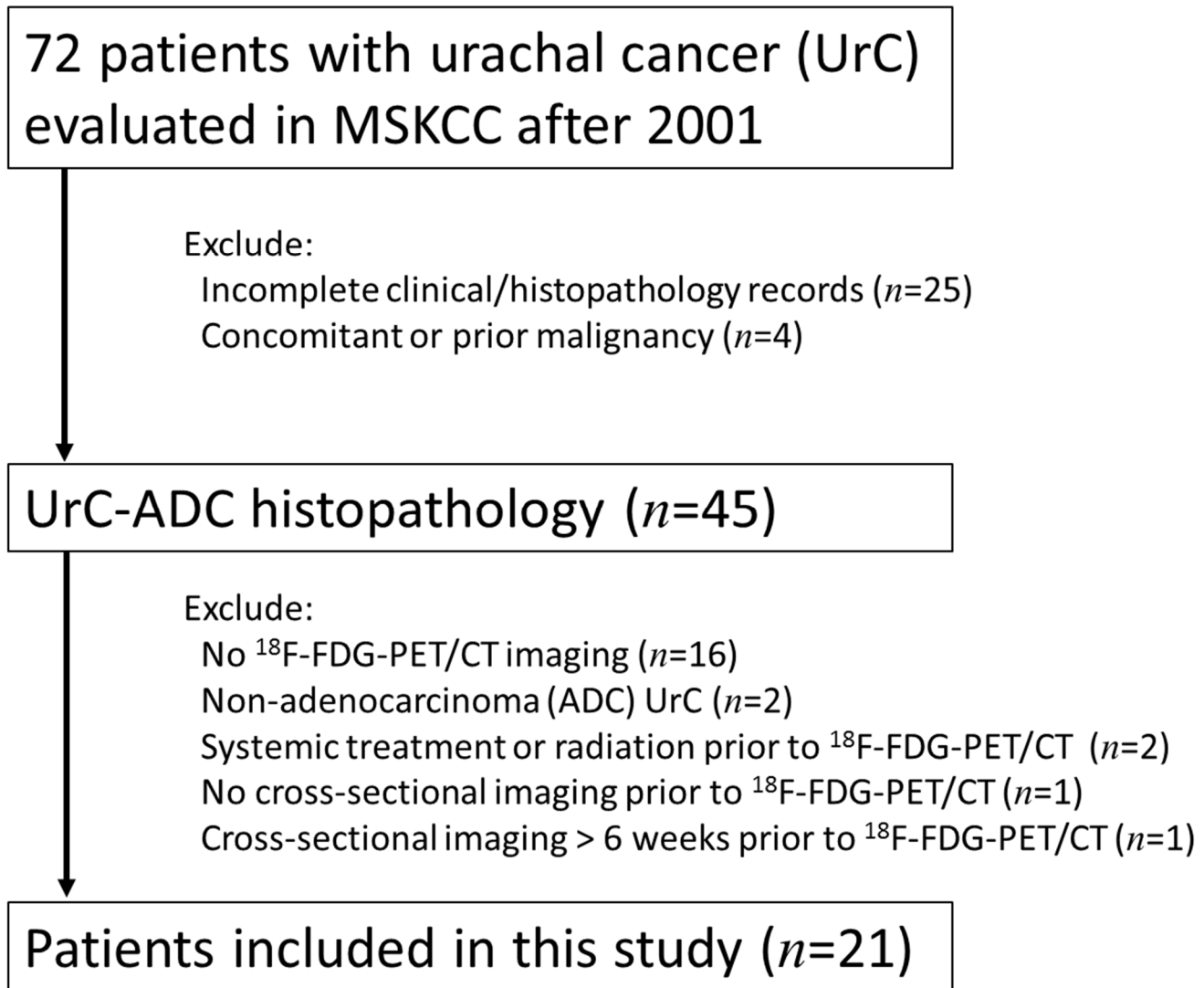


Figure 1. STARD diagram for patients screened and included in our analysis

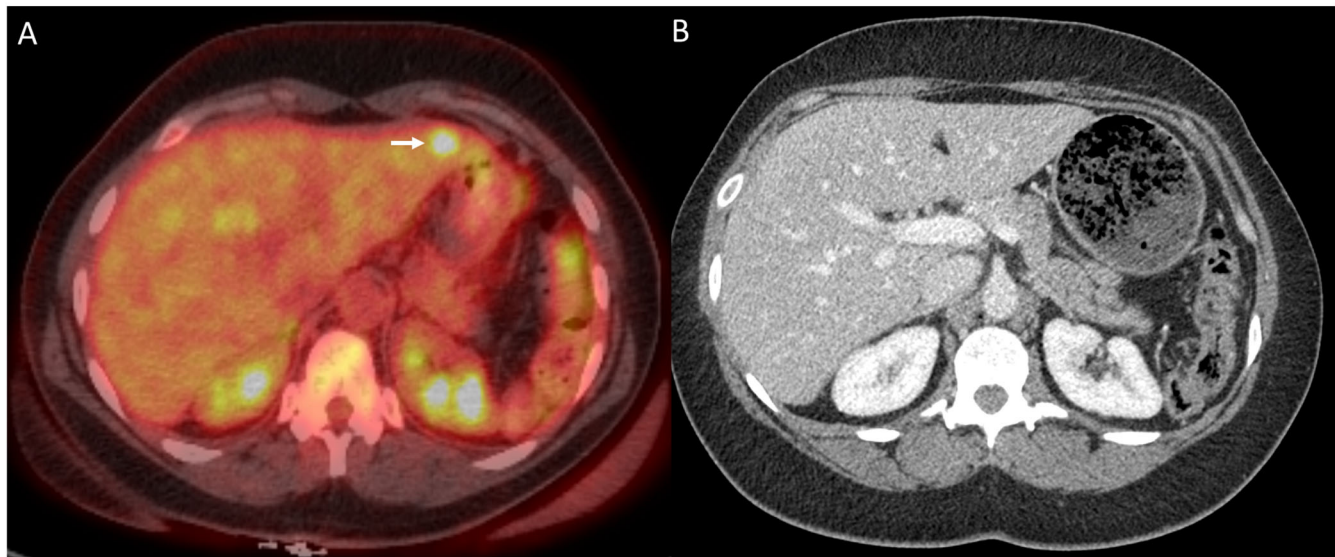


Figure 2. A 50-year-old male with a UrC-ADC. Axial fused ^{18}F -FDG-PET/CT (A) demonstrates an hepatic lesion (arrow), SUV_{max} 9.0, occult on prior CECT (B). The hepatic lesion was subsequently biopsied under ultrasound-guidance and proven to be a metastasis.

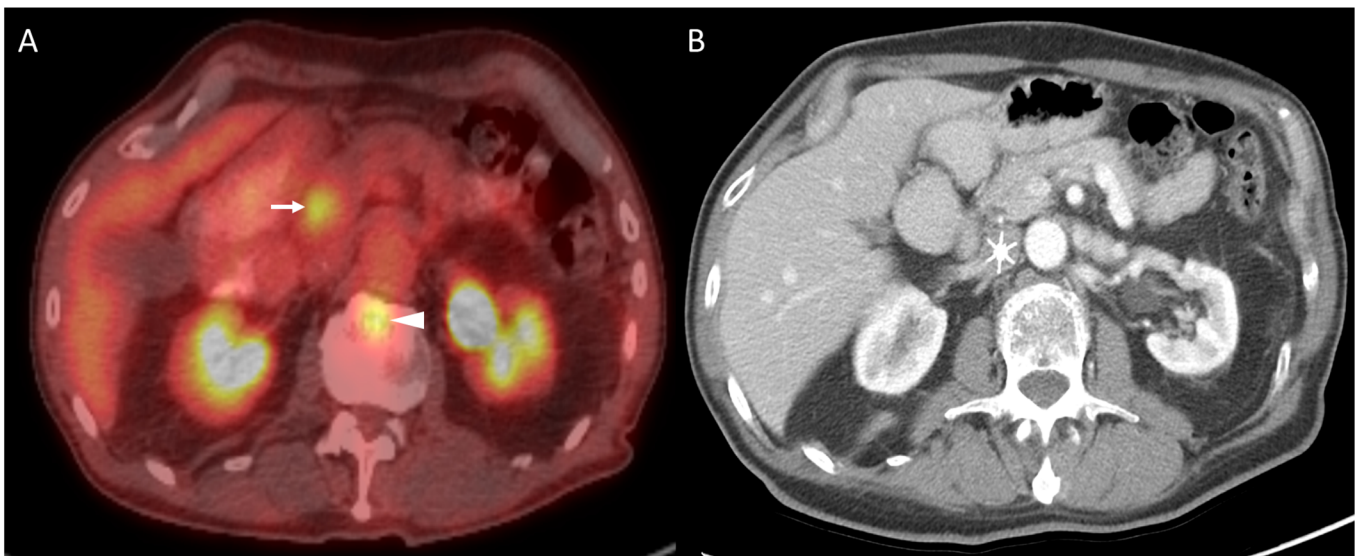


Figure 3. A 47-year-old male with a UrC-ADC. Axial fused PET/CT (A) demonstrates an FDG-avid pancreatic lesion (arrow), SUV_{max} 14.2, and additional osseous metastasis lesion (arrow head) not detected on prior CECT of the abdomen and pelvis (B). The pancreatic lesion was subsequently sampled by endoscopic ultrasound using fine needle aspiration and proven to be a metastasis.

RESULTS

Characteristics of primary UrC-ADC tumors on CECT and ¹⁸F-FDG PET/CT

The primary UrC-ADC tumor was imaged with CECT in 17 patients at the time of their initial clinical presentation. Mean size of the primary tumor measured in longest axis dimension was 4.8cm (range 2.2-13.7cm). Most tumors had well-defined margins (82%), were predominantly cystic or mixed solid-cystic (76%) and demonstrated enhancement (88%). 13 (76%) of the primary UrC-ADC tumors contained calcifications.

Six patients had their primary tumor resected prior to the immediate contrast-enhanced cross-sectional imaging (CT or MRI) study that preceded the ¹⁸F-FDG-PET/CT imaging study (performed \leq to 6 weeks after). That left 11 primary urachal tumors imaged on PET/CT. Seven of the 11 (63.6%) of the primary UrC-ADCs evaluable on PET/CT were FDG-avid, mean SUV_{max} 13.8 (range 4.0-27.5) and 4/11 (46%) demonstrated background FDG-uptake. Additional imaging features of primary urachal adenocarcinomas on CECT and ¹⁸F-FDG-PET/CT are summarized in **Supplemental Table 1**.

Mucinous tumors vs non-mucinous tumors and FDG avidity

Fourteen UrC-ADC were mucinous on histopathology. Of these, 10 of 14 (71%) had metastatic disease. Seven of 10 (70%) with metastatic disease demonstrated FDG-avid metastases. Of the 7 with FDG-avid metastases, 4 had an evaluable primary tumor and 3 of 4 of the primary tumors were FDG-avid (SUV_{max} values of 4, 1.7, and 24.6).

Seven UrC-ADC were non-mucinous tumors. Of these, 5 of 7 (71%) had metastatic disease. All 5 with metastatic disease (100%) demonstrated FDG-avid metastases. Of the 5 with FDG-avid metastases, 3 had an evaluable primary tumor and all 3 of the primary tumors were FDG-avid (SUV_{max} values of 9, 19.5, and 27).

Features on CECT	(n=17)	(%)
Well or ill-defined		
Well-defined	14	82
Ill-defined	3	18
Solid or cystic		
Cystic	7	41
Solid	4	24
Mixed (solid-cystic)	6	35
Enhancement		
Yes	15	88
No	2	12
Calcification		
Yes	13	76
No	4	24
Features on FDG PET/CT (n=11)		
FDG avid		
Yes	7	64
No	4	36

SUV_{max} of 7 avid primaries (median 13.8, range 4 -27.5)

Supplemental table 1. Imaging features of the primary UrC-ADC tumors on CECT and ¹⁸F-FDG PET