Title: Pilot study to assess the clinical utility of F-18 fluciclovine PET for cervical and endometrial cancer compared with F-18 FDG PET

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Axumin™ (fluciclovine F 18) Research Concept Proposal

Name & contact information	**Principal Investigator**	**Alternate Contact**
	Nghi C. Nguyen, MD, PhD Assistant Professor of Radiology University of Pittsburgh UPMC Presbyterian 200 Lothrop Street (at Meyran Ave) East Wing, 2nd Floor, Suite 200 Pittsburgh, PA 15213 Phone: 412-647-0104	
Institution	Department of Radiology. University of Pittsburgh Medical Center (UPMC), Pittsburgh, Pennsylvania	
Study Title	Pilot study to assess the clinical utility of F-18 fluciclovine PET for cervical and endometrial cancer compared with F-18 FDG PET	
Background/Rationale	Endometrial cancer arises from the inner lining of the uterus and is one of the most common malignancies in women, representing 3.6% of all new cancer cases in the US. It is estimated that there are more than 60,000 new cases of endometrial cancer and more than 10,000 people will die of this malignancy in 2016. It is most frequently diagnosed among women aged 55-64. Cervical cancer starts in the cervix, the lower part of the uterus. Its prevalence is lower compared with endometrial cancer thank to effective screening and early disease detection with the Pap smear. In 2016, it is estimated that there will be more than 12,000 new cases of cervical cancer and more than 4,000 patients will die of this disease in the US. Positron Emission Tomography (PET) combined with Computed Tomography (CT) is an essential part of workup for many malignancies. F-18 FDG PET/CT is being used clinically in the evaluation and management of pelvic malignancies in women. But there are certain diagnostic limitations related to F-18 FDG because it is mainly eliminated by the kidneys and often interferes with the detection of cancer lesion. On the other hand, the recently FDA approved F-18 fluciclovine is not be eliminated by the kidneys and therefore the image interpretation is not affected by nonspecific urine activity in the ureters and bladder, which is advantageous for pelvic imaging. Recent literature suggests that F-18 fluciclovine has diagnostic potential for a variety of solid tumors, thus, allowing new opportunities for noninvasive probing of glutamine metabolism and for clinical use in patient management. Current literature indicates that amino acid transporters including that of glutamine are upregulated in endometrial and cervical cancer, so F-18 fluciclovine PET may have clinical potential. The hypothesis is that F-18 fluciclovine PET provides better imaging properties and greater diagnostic confidence and accuracy than F-18 FDG PET in pelvic malignancies. Given the lack of current clinical data, a pilot study providing a direct comparison of F-18	

	fluciclovine PET with FDG PET is warranted. *(References: Cancer Res. 2014 Oct 15;74(20):5832-45. doi: 10.1158/0008-5472; J Biol Chem. 2016 Jun 17;291(25):13194-205. doi: 10.1074/jbc.M115.700534; Hum Pathol. 2011 Nov;42(11):1660-6. doi: 10.1016/j.humpath.2011.01.013*)
Study Objective(s)	We seek to conduct a pilot study to evaluate the clinical utility of F-18 fluciclovine for staging of cervical cancer and endometrial cancer. Our research will focus on the comparison of F-18 fluciclovine PET/MRI with the standard of care F-18 FDG PET/CT. Ten adult women with biopsy-proven endometrial cancer or cervical cancer scheduled for standard of care MRI of the pelvis for disease staging will be invited to participate in this research. Their clinical pelvic MRI scan will be performed on a PET/MR scanner (Siemens Biograph mMR) and combined with the research F-18 fluciclovine PET scan of the pelvis, with both MR and PET images acquired simultaneously. In addition, a whole-body PET/MR scan will be acquired for research only. The simultaneous PET/MR image acquisition is expected to provide significant improvement the TNM staging by combining the excellent soft-tissue contrast of MRI with F-18 fluciclovine PET, which is not affected by nonspecific urine activity in the ureters and bladder. The initial experience gained with this pilot study will provide valuable insights into the potential strengths and weaknesses of F-18 fluciclovine. The preliminary data will be used for sample size estimates for a R01 NIH grant application, which will validate the diagnostic accuracy as well as added value of F-18 fluciclovine PET compared with FDG PET/CT. In brief, the success of this pilot study will have significant implication for adopting F-18 fluciclovine PET for pelvic imaging in women.
Study Design (inclusion/exclusion criteria – patient population)	*Inclusion criteria:* Adult females with newly diagnosed endometrial and cervical cancer for whom an FDG PET/CT scan and a pelvic MR scan are being considered for disease staging. *Exclusion criteria:* Patients < 18 years; patients without biopsy proven malignancy of the endometrium or cervix; only FDG PET/CT scan or pelvic MR scan is being considered for standard of care imaging. An integrated PET/MR scanner which is operational at UPMC Presbyterian since Fall 2012 will be used for this research. Two PET scans will be performed – a regional scan of the pelvis in conjunction with the standard of care pelvic MRI with IV contrast and an additional whole-body scan PET/MR scan for research only. The total scan time on the PET/MR scanner is 30-45 minutes. The PET/MR data will be then correlated with the standard of care FDG PET/CT data, acquired within 2 weeks of the PET/MR scan.
Sample size and duration of follow-up	There have been no prior reports on the use of F-18 fluciclovine PET; thus, a sample size of 10 subjects would be sufficient for preliminary data collection.
Planned analyses	Research F-18 fluciclovine PET images and standard of care FDG PET images will be evaluated by two readers for image quality, lesion conspicuity and diagnostic confidence using visual scores. Semi-quantitative parameters of maximum lesion standardized-uptake-value (SUV) and background mean SUV will be obtained. Nonparametric statistical analyses will be used to compare the visual scores and SUV values between the two PET scans.

Timeframe for study start-up & duration of study	It is estimated that approximately 50 patients per year undergo FDG PET/CT and pelvic MR scans for disease staging at our referral center (Magee-Women's Hospital of UPMC). Clinical PET/MR workflows for tumor imaging including the pelvis are in place, and technical staff is trained to perform clinical PET/MR scans. Close research collaborations exist between Radiology and Radiation Oncology at Magee-Women's Hospital from where patients will be referred for this research. It takes about 3 months to get the IRB approved. Estimated start-up time is 5 months; the duration for the study is 12 months.
Support requested	I am requesting free supply for the 10 F-18 fluciclovine doses and 20% salary support for a research coordinator for this 12-month project. The standard of care pelvic MRI will be billed to the patients' health insurance.
Other source(s) of funding	The Department of Radiology would fund the scanner time incurred by the additional whole-body PET/MR scan (20-30 minutes).

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Please complete all relevant fields and email to Karen Linder, PhD, Sr Manager, Clinical Science and Medical Affairs.

Contact Information: **k.linder@blueearthdx.com**
O: +1-609-751-0587
M: +1-609-608-6455