

## **A tale of 3 tracers: Contrasting uptake patterns of <sup>18</sup>F-fluciclovine, <sup>68</sup>Ga-PSMA, and <sup>18</sup>F-FDG in the uterus and adnexa**

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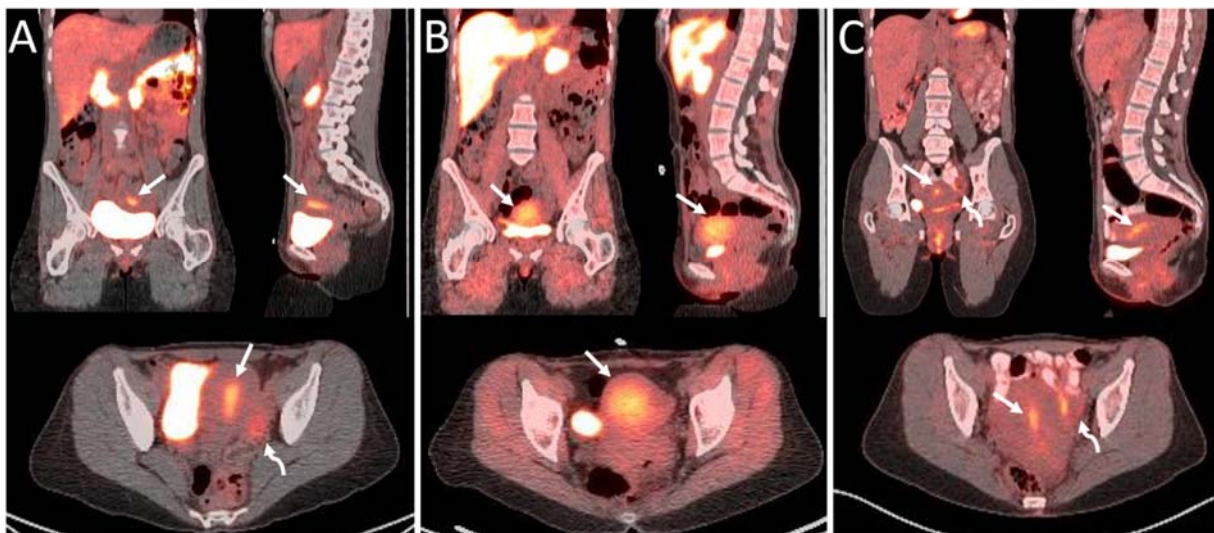
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**Abstract:** A 41-year-old woman with newly diagnosed invasive lobular carcinoma of the breast underwent sequential  $^{68}\text{Ga}$ -PSMA-11 PET/CT and  $^{18}\text{F}$ -fluciclovine PET/CT as part of an ongoing clinical trial (NCT04750473).  $^{68}\text{Ga}$ -PSMA PET/CT showed increased radiotracer uptake in the uterine endometrium and left adnexa.  $^{18}\text{F}$ -fluciclovine PET/CT showed increased radiotracer uptake in an enlarged uterus in a known uterine leiomyoma. A clinical  $^{18}\text{F}$ -FDG PET/CT demonstrated radiotracer uptake in the endometrium and a circumferential area of uptake in the left adnexa, a pattern more similar to the  $^{68}\text{Ga}$ -PSMA uptake pattern. This case highlights the discordance in the uptake pattern of two radiotracers in different benign gynecological conditions. While these tracers are approved for prostate cancer imaging, they are increasingly being used in other malignancies.

**Key words:**  $^{68}\text{Ga}$ -PSMA PET,  $^{18}\text{F}$ -fluciclovine PET, uterine leiomyoma, luteal cyst, endometrium, adnexa mass



**Figure 1.** A 41-year-old woman with newly diagnosed invasive lobular carcinoma of the right breast was enrolled into a clinical trial comparing the performance of  $^{68}\text{Ga}$ -PSMA-11 and  $^{18}\text{F}$ -

fluciclovine PET/CT in lobular breast cancer.  $^{68}\text{Ga}$ -PSMA PET/CT images of the patient (A) showed increased radiotracer uptake in the endometrium (straight arrows) and in the left adnexa (curved arrow). There is no significant  $^{68}\text{Ga}$ -PSMA uptake in the uterine myometrium. A review of the menstrual history of the patient revealed that she was in the secretory phase of her cycle during the PET/CT scans, suggesting that the endometrial and left adnexal uptake are related to ovulation. By contrast,  $^{18}\text{F}$ -fluciclovine PET/CT images (B) acquired 24 hours after the  $^{68}\text{Ga}$ -PSMA PET/CT study showed increased radiotracer uptake in the myometrium (arrows). The patient has a history of uterine leiomyoma.  $^{68}\text{Ga}$ -PSMA and  $^{18}\text{F}$ -fluciclovine are approved for prostate cancer imaging.<sup>1,2</sup> Yet, both radiotracers are not prostate cancer-specific and are increasingly being evaluated in other malignancies.<sup>3-5</sup> PSMA is expressed in the neovasculature of tumors, including endometrial carcinoma.<sup>6</sup> However, the homogeneous  $^{68}\text{Ga}$ -PSMA uptake in the endometrium and adnexa of this patient without clinical suspicion of endometrial carcinoma is similar to the known pattern of  $^{18}\text{F}$ -FDG uptake in the uterus and adnexa during the different phases of the menstrual cycle - a mid-cycle ovulatory phase rise in endometrial uptake with a subsequent decline and a luteal phase increased ovarian uptake.<sup>7,8</sup> In (C),  $^{18}\text{F}$ -FDG PET/CT images of this patient obtained four days after the  $^{18}\text{F}$ -fluciclovine PET/CT scan showed increased radiotracer uptake in the endometrium (straight arrows) and circumferential area of uptake in the left adnexa (curved arrows), demonstrating a pattern of uptake similar to the pattern seen on the  $^{68}\text{Ga}$ -PSMA PET/CT images. No significant uptake of  $^{18}\text{F}$ -fluciclovine is seen in the endometrium or the adnexa while  $^{18}\text{F}$ -FDG and  $^{68}\text{Ga}$ -PSMA PET/CT showed no significant radiotracer uptake in the leiomyomatous myometrium. This contrasting patterns of uptake between these three radiotracers is probably driven by the difference in the target engagement of the two radiotracers.  $^{18}\text{F}$ -fluciclovine is a radio-halogenated synthetic amino acid with known time-dependent physiologic uptake in muscles.<sup>9</sup> Since leiomyoma is a benign tumor of the uterine smooth muscle cells,  $^{18}\text{F}$ -fluciclovine uptake in it is congruent with the bio-distribution of the radiotracer. Increased  $^{18}\text{F}$ -PSMA-1007 has been previously reported in corpus luteal cyst.<sup>10</sup> This case, for the first time, presents a contrasting pattern of uptake of  $^{68}\text{Ga}$ -PSMA and  $^{18}\text{F}$ -fluciclovine and their relationship with the well-known uptake pattern of  $^{18}\text{F}$ -FDG in different benign gynecological conditions. The two radiotracers ( $^{68}\text{Ga}$ -PSMA and  $^{18}\text{F}$ -fluciclovine), which are commonly used in prostate cancer imaging, have the potential for use in imaging gynecological malignancies. Also,  $^{18}\text{F}$ -FES, a PET radiotracer that targets the estrogen receptor, was recently approved for breast cancer imaging. Uptake of  $^{18}\text{F}$ -FES in the endometrium (more in the proliferative phase than luteal phase) and the myometrium has also being reported.<sup>11,12</sup> Because cancerous and non-cancerous entities can co-occur, a working knowledge of the behavior of these tracers in non-malignant conditions is necessary to inform the accurate interpretation of PET/CT scans with these tracers acquired for oncological indications.



**Figure 2.** A contrast-enhanced CT (C) acquired 5 days prior to the  $^{68}\text{Ga}$ -PSMA PET/CT scan demonstrating leiomyoma of the uterus and left adnexa, identified as a luteal cyst. This left luteal cyst corresponds to the area of diffuse  $^{68}\text{Ga}$ -PSMA uptake and circumferential  $^{18}\text{F}$ -FDG uptake on the respective PET/CT scans.

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