Original Article

Acta Radiologica
2021, Vol. 62(9) 1257–1262
© The Foundation Acta Radiologica 2020
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/0284185120958404
journals.sagepub.com/home/acr

# Computed tomography contrast enhancement pattern of the uterus in premenopausal women in relation to menstrual cycle and hormonal contraception

**Konstantinos Angelopoulos[1,*], Magnus Palmér[1,*], Berit Gull[2], Niklas Lundqvist[1], Linda Kopelia[3], Mikael Hellström[1,4] and Henrik Leonhardt[1]**

## Abstract

**Background:** There are different types of computed tomography (CT) contrast enhancement patterns of the uterus. It is not known whether these are hormonally dependent.

**Purpose:** To assess the relationship between these patterns and the menstrual cycle in non-users of hormonal contraception, and the possible impact of hormonal contraception.

**Material and Methods:** Prospective observational study of abdominal CT scans of 53 premenopausal women of whom 28 were non-users and 25 users of hormonal contraception. The non-users were divided according to menstrual cycle phase: follicular (n = 12); ovulatory (n = 1); and luteal (n = 12). The pattern and intensity of contrast enhancement of the uterine myometrium were assessed.

**Results:** The dominant pattern of contrast enhancement of the myometrium was the diffuse homogeneous type in both non-users and users. The intensity of the enhancement measured in Hounsfield units (HU) was higher in the follicular phase (median 102, range 73–130) compared to the luteal phase in non-users (median 92, range 57–130); however this was not statistically significant ($P = 0.2$). The HU values observed in users (median 95, range 45–160) were at the same levels compared to those of the luteal phase in non-users.

**Conclusion:** The dominant pattern of contrast enhancement in the portal venous phase of the myometrium in fertile ages is the diffuse homogeneous type and is independent of menstrual cycle phase or the use of hormonal contraception. However, these factors seem to play a role in the intensity of contrast enhancement, with a tendency of higher HU values in the follicular phase of non-users.

**Keywords**

Uterus, computed tomography, contrast medium, radiographic image enhancement, menstrual cycle phases

Date received: 31 July 2020; accepted: 23 August 2020

## Introduction

Transvaginal ultrasound is the first-line imaging method for the examination of the female pelvis and the assessment of gynecologic disorders. Ultrasound can be combined with Doppler, and endometrial/subendometrial perfusion has been studied with this technique (1–3).

Magnetic resonance imaging (MRI) is an alternative diagnostic method with excellent intrinsic tissue contrast resolution. The uterine anatomy (4–8) and the perfusion of the myometrium observed on dynamic

[1]Department of Radiology, Sahlgrenska University Hospital, Gothenburg, Sweden
[2]Department of Gynecology, Sahlgrenska University Hospital, Gothenburg, Sweden
[3]Department of Medicine, National and Kapodistrian University of Athens, Athens, Greece
[4]Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden

*Equal contributors.

**Corresponding author:**
Henrik Leonhardt, Department of Radiology, Sahlgrenska University Hospital, Bruna straket 11B, 413 45 Gothenburg, Sweden.
Email: henrik.leonhardt@vgregion.se

contrast-enhanced MRI (9,10) have been described in detail in MRI studies.

Computed tomography (CT) is an inferior modality for imaging the internal genital organs in women, but is used for staging purposes in gynecologic cancers. Inevitably, the uterus is imaged as part of any abdominal/pelvic CT performed for different indications in women with preserved uterus and the radiologist has to be familiar with the organ's normal appearance and any significant deviation detected. However, there is a relative lack of data concerning the normal uterine anatomy and vascularity as depicted in CT scans.

Four different patterns of iodine contrast medium enhancement of the uterus in women that underwent abdominal CT for indications other than gynecologic have been described in the literature (12,13). Type 1 consists of bandlike subendometrial enhancement with or without enhancement of the outer myometrium 30–120 s after injection and has been described as occurring predominantly in premenopausal women. The zone of enhancement can be thick or thin. In Type 2, there is relatively homogenous contrast enhancement of the myometrium without bandlike enhancement in the arterial or parenchymal phases, found equally in pre- and postmenopausal women. In Type 3, there is a faint diffuse myometrial enhancement exclusively seen in postmenopausal women. As a fourth type, a patchy heterogeneous enhancement of the entire myometrium has been described (13). It has been observed that Type 1 enhancement progresses to diffuse myometrial enhancement at predominantly delayed phase imaging, in all women (13).

In the female reproductive system, cyclical angiogenesis occurs related to the physiological changes of each phase of the menstrual cycle (15,16). In CT studies of uterine contrast enhancement (13), the age and menopausal status of the individuals are considered to be the most important factors affecting the enhancement pattern; however, this has not been studied in detail in menstruating women. To our knowledge, there are no data correlating the phases of the menstrual cycle to the CT contrast enhancement pattern of the uterus.

In ultrasound studies, women with subfertility of unknown etiology have been described as presenting differences in endometrial and subendometrial vascularity as well as in the uterine artery kinetics compared to the controls (1,14). This leads to the assumption that an unexpected contrast enhancement pattern observed on a CT scan could be indicative of a clinically significant perfusion abnormality. In order to understand such perfusion abnormalities, the normal contrast enhancement pattern during the different phases of the menstrual cycle needs to be defined. It is well-known that leiomyomas, malignant uterine tumors, and other pathological conditions may show a different contrast enhancement compared to the normal uterus. Knowledge of the normal perfusion patterns can lead to a better understanding of the pathophysiology and an improved diagnostic ability.

The aim of the present study was to examine the possible relationship between the myometrial contrast enhancement pattern and the phases of the menstrual cycle, and to examine the use of hormonal contraception.

## Material and Methods

This prospective observational study was conducted between May 2016 and December 2017 at Sahlgrenska University Hospital and was performed in accordance with the declaration of Helsinki and approved by the Regional Ethics Committee at the Regional Ethics Committee at the University of Gothenburg, Sweden (D-No. 117–16).

### *Participants*

Fifty-three premenopausal women (median age = 35 years; age range = 19–48 years) were consecutively included. They all underwent abdominal CT scans for diagnostic purposes, on indications not related to the reproductive system. Exclusion criteria were: pregnancy or an interval of less than two months between childbirth and the CT; lactation; oligomenorrhea in non-users of hormonal contraception; and known gynecological diseases that can affect the imaging characteristics of the uterus, such as malignancy, leiomyomas, and adenomyosis.

Before the CT examination, the participants provided written informed consent as well as written information of their menstrual cycle (duration, regularity, and date of last menstruation), previous pregnancies, chronic diseases, usage and type of contraception as well as any other medication.

The participants were divided into users and non-users of hormonal contraception. The first group was further divided according to the phase of menstrual cycle. Day 1 was defined as the first day of menstruation. The follicular phase included days 1–13, the ovulatory phase days 14–16, and the luteal phase days 17–28 (17).

### *CT technique*

The abdominal–pelvic CT scans were performed after intravenous administration of 0.5 g/kg (50–80 kg) iodine contrast medium with a concentration of 350 mgI/mL (Iomeron®, Bracco Imaging Scandinavia, Gothenburg, Sweden) and rate of injection of 14.3 mgI/kg/s. The scan delay was 80 s and all scans were performed with 120 kV and Exposure Dose Modulation in order to give the same image quality with similar Noise Index and reference mAs. The CT scanners used had 64-slice detectors with collimation of 40 mm (Goldseal Optima CT660/Discovery CT750HD GE Health Care, Chicago, IL, USA/Siemens Definition DS, Siemens Healthineers, Erlangen, Germany/Aquilion Prime, Canon Medical Systems, Tochigi, Japan). The pitch value was set to 1.0 as reference pitch. Batches of axial images with a thickness of 5 mm and increment of 5 mm, and coronal and sagittal reconstructions with a thickness of 4 mm and increment of 3 mm increment were saved in the PACS for review. The attenuation of the contrast-enhanced myometrium was measured as follows: a 40-$mm^2$ ROI was placed in the anterior and posterior wall, respectively, of the central-outer myometrium and the mean Hounsfield unit (HU) value was calculated.

### *Classification*

The enhancement pattern was classified as Type 1–4 based on the system described by Yitta et al. (Figs. 1–4) (13):

- *Type 1*: Subendometrial bandlike enhancement with or without outer myometrial enhancement.
- *Type 2*: Enhancement progressing from the outer myometrial region to the entire myometrium or diffuse from the onset, without any defined subendometrial enhancement.
- *Type 3*: Faint diffuse myometrial enhancement.
- *Type 4*: Patchy heterogeneous enhancement throughout the myometrium.

The characterization of the enhancement pattern and the HU measurements were carried out by a radiology resident (KA) with four years of experience in abdominal CT. Cases that were considered difficult to interpret were evaluated in consensus with an experienced radiologist (HL), with 25 years of experience in abdominal CT.

### *Statistical methods*

The Stata 15 statistical package (StataCorp LLC) was used for statistical analysis. One-way analysis of variance (ANOVA) and Chi-square test were performed, and a significance level of 5% was used.

## Results

Twenty-eight patients (median age = 37 years; age range = 19–48 years) were included in the group of non-users of hormonal contraception and 25 patients (median age = 30 years; age range = 20–45 years) were included in the group of users. The distributions according to menstrual cycle phase within the non-user and the user groups are presented in Table 1, along with the different types of contrast enhancement. The dominant type of enhancement was Type 2, observed in 45/53 (85%) participants; in 24 (86%) non-users and in 21 (84%) users of hormonal contraception. In more detail, we found that in non-users the observed Type 2 pattern was exclusively that of direct diffuse homogeneous enhancement, whereas four of the 21 users with Type 2 pattern presented outer myometrial enhancement (Fig. 1). Of the 12 women in the follicular phase, 11 (92%) presented Type 2 enhancement, as well as the one participant who was in the ovulatory phase and 10/12 (83%) women in the luteal phase.

A difference in appearance of the rare Type 1 bandlike subendometrial enhancement pattern between the two groups was noticed. In non-users, enhancement of a thick subendometrial zone was observed, whereas in users, enhancement of a thin zone was observed.

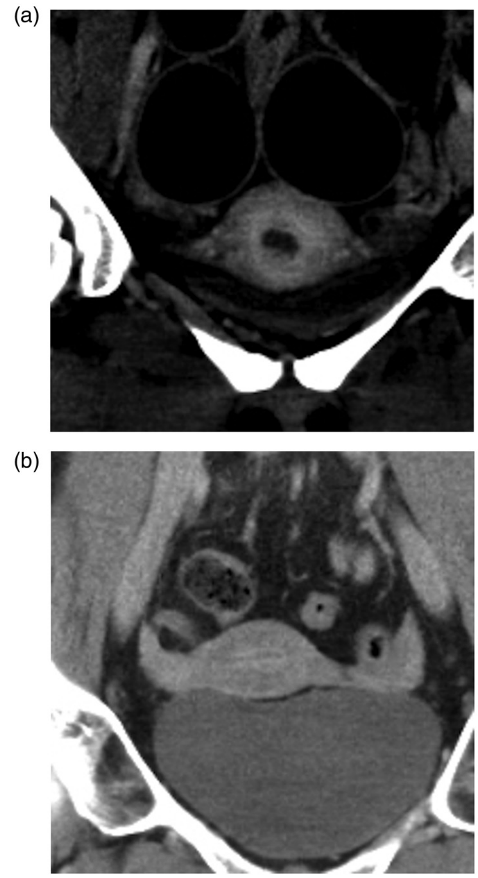

**Fig. 1.** (a) Coronal abdominal CT scan of a non-user of hormonal contraception with enhancement of the thick subendometrial zone (Type 1) and (b) coronal abdominal CT scan of a user of hormonal contraception presenting contrast enhancement of the thin subendometrial zone (Type 1).

(a)
(b)

**Fig. 2.** (a) Coronal and (b) sagittal abdominal CT scan presenting homogeneous contrast medium enhancement of the myometrium (Type 2).

**Fig. 3.** Sagittal abdominal CT scan showing faint diffuse enhancement (Type 3) of the myometrium.

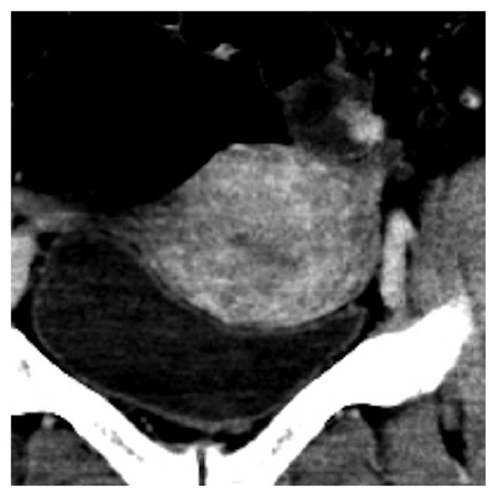

**Fig. 4.** Heterogeneous contrast enhancement (Type 4) of the myometrium seen in a coronal abdominal CT scan.

Type 2 was the dominant pattern regardless of whether the women had born children (Table 2).

The measurements of myometrial attenuation were in the range of 45–160 HU; details are listed in Table 3. There was a tendency of higher attenuation in the follicular phase (median = 102, range = 73–130) compared to the luteal phase in non-users (median = 92, range = 57–130); however, this was not statistically significant ($P = 0.2$). The HU values observed in users were at the same levels compared to those of the luteal phase in non-users.

Sub-analyses were also performed in stratified groups regarding age, body mass index, and type of contraceptive hormonal medication (gestagen vs. combinations of hormones), but no significant differences were observed (data not shown).

**Table 1.** Types of contrast enhancement of the myometrium in non-users (n = 28) and users (n = 25) of hormonal contraception.

| | Type 1 | Type 2 | Type 3 | Type 4 |
|---|---|---|---|---|
| Non-users | | | | |
| Follicular phase | 1 | 11 | – | – |
| Ovulatory phase | – | 1 | – | – |
| Luteal phase | – | 10 | 1 | 1 |
| Unknown phase | 1 | 2 | – | – |
| Users | 3 | 21 | 1 | 0 |

## Discussion

In abdominal CT scans performed in the portal venous phase of consecutive non-gynecologic patients, we observed that the Type 2 contrast medium enhancement pattern of the uterus is the dominant pattern in users and non-users of hormonal contraception. It is the dominant pattern in every phase of the menstrual

**Table 2.** Enhancement type of the myometrium and frequency of previous births in non-users and users of hormonal contraception.

| | Primi/multiparous | Nulliparous |
|---|---|---|
| Type 2, non-users | 15 | 9 |
| Type 2, users | 8 | 13 |
| Non-type 2, non-users | 3 | 1 |
| Non-type 2, users | 3 | 1 |

**Table 3.** Myometrial contrast medium enhancement attenuation values observed in users and non-users of hormonal contraception.

| | Attenuation value (HU) | *P* value |
|---|---|---|
| Non-users | | |
| Follicular phase | 102 (73–130) | |
| Ovulatory phase | 120 (–) | |
| Luteal phase | 92 (57–130) | 0.2 |
| Users | 95 (45–160) | 0.2 |

Values are given as median (range).
One-way analysis of variance was used to estimate the statistical significance of the difference in attenuation between the follicular phase and the luteal phase and between the follicular phase and users.

cycle. In accordance with previous data collected from MRI perfusion studies, we observed a trend of more intense enhancement of the myometrium in the follicular and ovulatory phases compared to the luteal phase (9–11). However, the difference was not statistically significant, perhaps due to the relatively small sample size.

The low number of Type 1 pattern in the present study may be due to the fact that all examinations were performed in the portal venous phase and none in the arterial phase. The subendometrial bandlike enhancement in Type 1 has been described to be transient and progress to diffuse enhancement of the myometrium at delayed phase imaging (12,13).

All the non-users with the Type 2 pattern presented diffuse homogeneous enhancement throughout the entire myometrium. Some of the users (19%) with the Type 2 pattern presented a more intense enhancement of the outer myometrium, which theoretically could be a result of reduced perfusion in the subendometrial layer (junctional zone) caused by hormonal contraception. It has been shown that the junctional zone is thinner in users compared to non-users and one can assume that this difference is also indicative of reduced perfusion (8). The present study also indicates that the use of hormonal contraception results in reduced thickness of the junctional zone as the Type 1 enhancement pattern in users was that of thin bandlike enhancement compared to thick bandlike enhancement that was exclusively observed in non-users; however, this conclusion is uncertain due to the low numbers observed.

Patterns other than Type 2 in the user group were observed more often in women with previous pregnancies: 3/4 (75%) of them were mothers compared to eight mothers out of 21 women (38%) that presented with the Type 2 pattern. Although the difference was not statistically significant ($P = 0.14$), there was a tendency for overrepresentation of patterns other than Type 2 in the subgroup of mothers in the user group; perhaps this would have been significant if the sample had been larger. However, we did not see the same tendency in the non-user group, which is an argument against the possible long-term effect of pregnancy and birth on the perfusion of the uterus. Larger series of patients are needed in order to determine whether previous pregnancies can affect the contrast enhancement of the myometrium and in what way.

We have used a classification system of uterine contrast enhancement pattern first presented by Kaur et al. (12). Three different types of patterns were described, but we added Type 4 (patchy heterogeneous) as suggested by Yitta et al. (13). Type 1 could possibly be further subdivided into thin/thick subendometrial enhancement or outer myometrial (subserosal) enhancement. Thus, this classification can be discussed and, to our knowledge, has not been further validated.

As far as we know, this is the first prospective study in the literature relating the CT iodine contrast medium enhancement pattern of the uterus to the phases of the menstrual cycle. The major limitation of the present study is the relatively small number of participants. This is partly due to the fact that CT, as a modality with a relatively high radiation dose to the patient, is avoided if possible for elective indications in women of fertile ages in favor of ultrasound and MRI. Radiation and possible hazards of iodine contrast medium would make a study design using healthy volunteers unethical. A further limitation is that no hormonal levels were available for the precise determination of the phase of the menstrual cycle of the participants. Although different CT machine types were used, we have not studied the reproducibility of the classification.

In conclusion, the dominant pattern of CT contrast enhancement in the portal venous phase of the uterus is of the diffuse homogeneous enhancement type and is independent of the menstrual cycle or the use of hormonal contraceptives. The phases of the menstrual cycle seem to play a role in the intensity of the observed contrast enhancement in non-users of hormonal contraceptives; this was highest in the follicular phase, although the difference compared to the luteal phase did not reach statistical significance. In women using hormonal contraception, the myometrial contrast enhancement is similar to the lower enhancement in the luteal phase of non-users. Thus, in general, a homogenous contrast enhancement of the myometrium can be expected in CT examinations performed in the portal venous phase of women in fertile ages. Other patterns or irregular contrast enhancement in this phase could be indicative of uterine disorders but this needs to be further investigated in future studies.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) received the following financial support for the research, authorship, and/or publication of this article: This work was supported by the ALF-agreement; The Healthcare Committee, Region Västra Götaland (Hälso- och sjukvärds-styrelsen) [grant number ALFGBG-875241].

## ORCID iDs

Mikael Hellström https://orcid.org/0000-0003-4031-332X
Henrik Leonhardt https://orcid.org/0000-0003-2209-6130

## References

1. Raine-Fenning NJ, Campbell BK, Kendall NR, et al. Endometrial and subendometrial perfusion are impaired in women with unexplained subfertility. Hum Reprod 2004;19:2605–2614.
2. Raine-Fenning NJ, Campbell BK, Kendall NR, et al. Quantifying the changes in endometrial vascularity throughout the normal menstrual cycle with three-dimensional power Doppler angiography. Hum Reprod 2004;19:330–338.
3. Jokubkiene L, Sladkevicius P, Rovas L, et al. Assessment of changes in endometrial and subendometrial volume and vascularity during the normal menstrual cycle using three-dimensional power Doppler ultrasound. Ultrasound Obstet Gynecol 2006;27:672–679.
4. Hricak H, Alpers C, Crooks LE, et al. Magnetic resonance imaging of the female pelvis: initial experience. AJR Am J Roentgenol 1983;141:1119–1128.
5. Brown HK, Stoll BS, Nicosia SV, et al. Uterine junctional zone: correlation between histologic findings and MR imaging. Radiology1991;179:409–413.
6. Hricak H, Kim B. Contrast-enhanced MR imaging of the female pelvis. J Magn Reson Imaging 1993;3:297–306.
7. McCarthy S, Scott G, Majumdar S, et al. Uterine junctional zone: MR study of water content and relaxation properties. Radiology 1989;171:241–243.
8. Meylaerts LJ, Wijnen L, Grieten M, et al. Junctional zone thickness in young nulliparous women according to menstrual cycle and hormonal contraception use. Reprod Biomed Online 2017;34:212–220.
9. Thomassin-Naggare I, Balvay D, Cuenod CA, et al. Dynamic contrast-enhanced MR imaging to assess physiologic variations of myometrial perfusion. Eur Radiol 2010;20:984–994.
10. Meylaerts LJ, Wijnen L, Bazot M, et al. Perfusion of the uterine junctional zone in nulliparous and primiparous women assessed by DCE-MRI, as a function of menstrual cycle and hormonal contraception. J Magn Reson Imaging 2017;38:101–111.
11. Thomassin-Naggara I, Siles P, Balvay D, et al. MR perfusion for pelvic female imaging. Diagn Interv Imaging 2013;94:1291–1298.
12. Kaur H, Loyer EM, Minami M, et al. Patterns of uterine enhancement with helical CT. Eur J Radiol 1998;28:250–255.
13. Yitta S, Hecht EM, Mausner EV, et al. Normal or Abnormal? Demystifying Uterine and Cervical Contrast Enhancement at Multidetector CT. Radiographics 2011;31:647–661.
14. Steer CV, Tan SL, Mason BA, et al. Midluteal-phase vaginal color Doppler assessment of uterine artery impedance in a subfertile population. Fertil Steril 1994;61:53–58.
15. Gargett CE, Rogers PAW. Human endometrial angiogenesis. Reproduction 2001;121:181–186.
16. Fraser HM, Lunn SF. Angiogenesis and its control in the female reproductive system. Br Med Bull 2000;56: 787–797.
17. Wilcox AJ, Dunson D, Baird DD. The timing of the "fertile window" in the menstrual cycle: day specific estimates from a prospective study. BMJ 2000;18:1259–1262.