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# MRI analysis of uterine ischaemia as a form of non-target embolisation following uterine artery embolisation: incidence, extent and outcome

N.N.N. Naguib [a,b,1], B. Kaltenbach [c,1], A.A. Abdel-Karim [b], A. Elabd [b], H. Abd-Elsalam [b], R. Hammerstingl [c], H. Ackermann [d], T.J. Vogl [c], N.-E.A. Nour-Eldin [c,e,*]

[a] Department of Radiology, AMEOS Hospital Halberstadt, Germany
[b] Department of Diagnostic and Interventional Radiology, Faculty of Medicine, Alexandria University, Egypt
[c] Institute for Diagnostic and Interventional Radiology, Frankfurt University Hospital, Germany
[d] Department of Biomedical Statistics, Frankfurt University Hospital, Germany
[e] Department of Diagnostic and Interventional Radiology, Cairo University, Egypt

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AIM: To study the incidence, extent and fate of uterine ischaemia as one of the forms of non-target embolisation following uterine artery embolisation (UAE), as detected on immediate post-embolisation and contrast-enhanced magnetic resonance imaging (MRI) examinations at the 3-month follow-up.

MATERIALS AND METHODS: A retrospective study was undertaken comprising 43 women (mean age: 44.8 ± 3.79 years). MRI was performed before, immediately after (within 6 h), and 3 months after successful UAE. Areas of uterine ischaemia were identified on immediate post-embolisation MRI as regions of newly developed (compared to pre-embolisation MRI) absent enhancement within the uterus not corresponding to the location of the leiomyoma. The volume of the ischaemic region was calculated using the formula (height × length × width × 0.523).

RESULTS: Uterine ischaemia was encountered in 29 patients (67.44%). The mean volume of the ischaemic region immediately after UAE was 29.29 ± 19.15 ml (range: 7.36–87.71 ml). At 3-month follow-up, it was 0.35 ± 0.95 ml (range: 0–3.5 ml) with 25 (86%) patients showing complete resolution of the ischaemia. The mean reduction in the volume of the ischaemic region at the 3-month follow-up was 98.24 ± 5.72% (range: 72–100%). This volume reduction was statistically significant ($p<0.0001$).

CONCLUSION: Uterine ischaemia as a form of non-target embolisation following UAE might be encountered in up to two thirds of patients. These ischaemic areas are significantly reduced at the 3-month follow-up with up to 86% of cases showing complete reversibility of the ischaemia.



* Guarantor and correspondent: N.-E. A. Nour-Eldin, Institute for Diagnostic and Interventional Radiology, Johann Wolfgang Goethe-University Frankfurt, Theodor-Stern-Kai 7, 60590 Frankfurt Am Main, Germany.
*E-mail address:* nour410@hotmail.com (N.-E.A. Nour-Eldin).
[1] These authors contributed equally to the present work.

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## Introduction

Since its first introduction in 1995[1] uterine artery embolisation (UAE) has established itself as one of the treatment options for treating symptomatic uterine leiomyoma.[2–4] Recently published results of the Cochrane database concluded that UAE provides short-term and mid-term patient satisfaction results comparable to myomectomy and hysterectomy.[5] Long-term follow-up studies showed comparable quality of life results between UAE and hysterectomy.[6]

During UAE embolisation, the catheter tip is placed in the main uterine artery beyond the cervico-vaginal branch.[7] As the leiomyoma supplying arteries are slightly larger than the arteries supplying the normal uterine tissue preferential flow of the injected embolising material is expected to occur and the arteries supplying the leiomyoma being larger are expected to be embolised first.[4] Although this is a theoretical hypothesis, some non-target embolisation of the normal uterine tissue will occur due to the relatively non-selective nature of the technique.

The rate of major complications following UAE is relatively low, a meta-analysis that included 8,159 patients estimated the rate of major complications to be 2.9%.[8] The reported major complications included angiography-related complications, infection, passage of fibroid tissue, pulmonary embolism or deep vein thrombosis, permanent amenorrhea and the need for hysterectomy due to complications. The reported rate of hysterectomy to treat complications of UAE was estimated to be 0.7% (26 out of 4,093 patients) and was collectively attributed to either uterine infection or ischaemia.[8] Uterine ischaemia following UAE has been sporadically reported in medical literature mostly as case reports[9–11] or in the context of discussing possible complications of UAE.[12] To our knowledge the medical literature contain insufficient data regarding the real incidence, extent, and outcome of uterine ischaemia following UAE. Based on this, the present study was performed to investigate the incidence, extent, and outcome of uterine ischaemia following successful bilateral UAE using contrast-enhanced MRI.

## Materials and methods

The study was approved by the ethical committee of the university hospital. Informed consent was obtained from all patients prior to UAE. The study was performed retrospectively and comprised 43 women (age range: 33–52 years, mean: 44.8 ± 3.79 year) in whom successful bilateral UAE was performed between March 2012 and March 2014.

### *Patient selection*

All patients suffered from symptomatic uterine leiomyomas and had previous failed medical treatment for at least 6 months prior to UAE. Included patients were all treated with successful bilateral UAE during the study time frame and underwent an MRI examination before (within 2 weeks before UAE), immediately after (within the first 6 h after UAE), and 3 months after UAE. Excluded were patients who did not return for follow-up and patients with general contraindications to contrast-enhanced MRI, e.g., history of severe allergy or hypersensitivity to contrast media.

### *UAE*

All interventional procedures were performed by a single team of two interventional radiologists with >20 and > 15 years of experience in interventional radiology. All procedures were performed successfully and both uterine arteries were embolised through a unilateral femoral puncture (right side in all cases). All procedures were performed using an Artis Zeego angiography suite (Siemens Healthcare, Forchheim, Germany). The right common femoral artery was punctured following local anaesthesia using Seldinger's technique and a 5 F sheath was inserted in the artery (Terumo, Tokyo, Japan). A 4 F Cobra C2 catheter (Terumo) was used to catheterise the contralateral uterine artery in all cases. The catheter was advanced in the uterine artery beyond the cervicovaginal branch. Embolisation was performed until stasis using Bead Block 500–700 μm (Terumo). A 5 F side-winder 1 (Terumo) catheter was used to catheterise and embolise the ipsilateral uterine artery either alone ($n$=31) or in combination with a micro-catheter (Renegade, Boston Scientific, Cork, Ireland; $n$=12). At the end of the intervention, the femoral puncture site was closed using a vascular closure device (Angioseal, St Jude Medical, St Paul, MN, USA). Patients were then transferred for observation and pain management using intravenous analgesics.

### *MRI*

All MRI examinations were performed using a 3-T MRI unit (Magnetom Trio, Siemens, Forchheim, Germany). MRI studies were performed within 2 weeks before UAE, during the first 6 h after and 3 months after UAE. The immediate post-interventional MRI was performed as a part of the departmental routine protocol for UAE.

A body-array coil was used to cover the region of interest and then the localiser was taken in three planes to localise the area of interest. Then, the MRI sequences were performed according to the following protocol. First a T2 half-Fourier axial single-shot fast spin-echo (HASTE) was performed in the coronal plane with a repetition time (TR) of 2,000 ms, echo time (TE) of 90, section thickness (ST) was 5 mm, field of view (FOV) was 380, and flip angle (FA) was 150°. This was followed by T2-weighted sequences in the coronal (TR/TE = 6,392 ms/121 ms, ST = 5, FOV 400, FA = 120°), transverse (TR/TE = 7,500 ms/121 ms, ST = 5, FOV = 400, FA = 120°) and sagittal (TR/TE = 5,462 ms/106 ms, ST = 5, FOV = 350, FA = 140°) planes. Then unenhanced T1-weighted images were taken in the transverse and sagittal planes (TR/TE = 589 ms/9.6 ms, ST = 5, FOV 400, FA = 150°). T1-weighted fat-suppressed images were taken in the transverse and sagittal planes (TR/TE = 609 ms/8 ms, ST = 5, FOV 350, FA 150°) following contrast

medium administration (Dotarem, Guerbet GmbH, Sulzbach, Germany) in a dose of (0.2 ml/kg body weight followed by 20ml normal saline) using an MRI compatible power injector (Spectris, Medrad, Pittsburg, PA, USA) with a flow rate of 3 ml/s.

*Image evaluation*

All MRI studies were evaluated by another two radiologists (with >10 and > 8 years of experience in gynaecological imaging) in consensus. The immediate post-UAE MRI examination was used to evaluate possible uterine ischaemia. In all cases, the T1 fat-suppressed contrast-enhanced axial and sagittal MRI sequences were used to identify the uterine ischaemia. Uterine ischaemia was defined as newly developed areas of absent contrast enhancement, as compared to the MRI examination before UAE, and not corresponding to the location of the uterine leiomyomas, as identified from the pre-embolisation MRI. The same criteria were used to identify residual areas of uterine ischaemia at 3-month MRI follow-up. For size evaluation the maximal diameter on the axial images was measured and identified as length, the width was measured perpendicular to the length and the height was measured in the cephalocaudal direction on the sagittal images. This was followed by volume calculation of the ischaemic area using the formula for ellipsoid lesions (length × width × height × 0.523). Volume measurements were performed on the immediate MRI examination and on the 3-month follow-up MRI. Volume assessment was selected in the present study to better demonstrate the whole extent of the ischaemic areas, which might be underestimated or overestimated if unidimensional or bidimensional measurements were used.

*Data collection and analysis*

The obtained volumes were tabulated for analysis. The mean ± standard deviation and range of volumes were obtained. The possible change in the volume of the uterine ischaemic area between the immediate and 3-month follow-up MRI was tested for statistical significance using the one-sample paired t-test. The correlation between the volume of the non-target ischaemic area and the percentage change at follow-up, the correlation between the volume of the embolic material used and the volume of the non-target ischaemic area in all patients and the percentage change in volume of the ischaemic area after 3 months were tested using Spearman rank correlation test. A $p$-value of $<0.05$ was considered statistically significant. All analysis was performed using BiAS for windows software.

## Results

UAE was performed successfully and bilaterally in all patients. The mean volume of the embolisation material used in all patients was 6.88 ± 2.20 ml (range 4–14 ml). On immediate post-embolisation MRI examination areas of uterine ischaemia were identified in 29 out of the 43 patients (67.4%). In all cases, the uterine ischaemia was seen as newly developed area of centrally located absent contrast enhancement involving the endometrium and myometrium and not corresponding to the location of the uterine leiomyomas (Fig 1). The mean volume of the ischaemic area on immediate MRI examination was 29.29 ± 19.15 ml (range: 7.36–87.71 ml). No statistically significant correlation was noted between the volume of the used embolic agent and the volume of the non-target ischaemic area in all patients (rho = 0.20, $p$=0.19).

*Outcome of uterine ischaemia*

At the 3-month follow-up, the previously identified uterine ischaemic area showed a mean volume of 0.35 ± 0.95 ml (range: 0–3.5 ml). Complete resolution of the uterine ischaemia was seen in 25 out of the 29 patients (86%) with complete revascularisation of the endometrial and myometrial ischaemic area (Fig 2). At the 3-month follow-up, the mean percentage reduction of the uterine ischaemic area was 98.24 ± 5.72% (range: 72–100%). The reduction in the volume of the ischaemic area at the 3-month follow-up was statistically significant ($p<0.0001$). No statistically significant correlation was noted between the volume of the embolic agent used and the percentage reduction of the uterine ischaemic area (rho = −0.12, $p$=0.53). In addition, no statistically significant correlation was noted between the volume of the non-target ischaemic area immediately after UAE and the percentage change at 3-month follow-up (rho = 0.05, $p$=0.79). This means that the initial size of the non-target ischaemic area did not influence the outcome of the ischaemic area.

Table 1 shows the measurements of the ischaemic area in all 29 patients who showed immediate post-embolisation non-target ischaemia. In addition, the table shows the volume of the ischaemic areas immediately after and 3 months after UAE.

## Discussion

Over the past 20 years, UAE has established itself as an effective and safe potential alternative to conventional surgical procedures for treating females with symptomatic uterine leiomyoma not responding to medical treatment.[8,13,14] The minimally invasive nature of the treatment, its low rate of major complications[15] and its ability to treat multiple uterine leiomyoma in a single session[16] gave this treatment option its attractiveness.

The technique of uterine artery embolisation entails a relatively non-selective form of embolisation where the catheter is placed in the main uterine artery beyond the origin of the cervico-vaginal branch.[7,17] The fact that the embolising material will be injected in the main stream of the uterine artery, even with the hypothesis of preferential flow into the relatively large leiomyoma vessels,[4] means that non-target embolisation of the normal uterine tissue is possible. Review of the medical literature shows very few reports addressing the subject. The discrepancy between the relative non-selectivity of the technique and the very

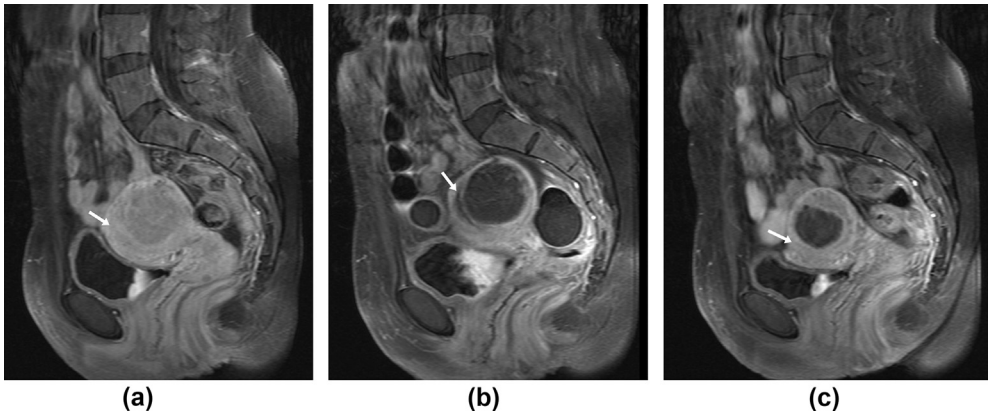


**Figure 1** (a) Pre-embolisation sagittal T1-weighted fat-suppressed MRI of a 41-year-old woman with symptomatic leiomyoma showing a posterior-wall leiomyoma with normal enhancement of the endometrium (white arrow). (b) MRI immediately following embolisation shows an ischaemic area of the endometrium (white arrow) seen as an area of non-enhancement anterior to the devascularised leiomyoma. (c) MRI at 3-month follow-up shows full resolution of the ischaemic area (white arrow) with normal enhancement of the endometrium.

low incidence of reporting such an encounter rendered a further investigation of the subject mandatory. The present study was undertaken to investigate the incidence of uterine ischaemia following UAE using contrast-enhanced MRI performed immediately following UAE. In order to make sure that the findings of uterine ischaemia are directly related to the procedure and that these areas are not related to the location of the leiomyoma, the findings were compared against the MRI studies performed within 2 weeks of embolisation. In accordance with the relative non-selectivity of UAE, the incidence of uterine ischaemia as a form of non-target embolisation was relatively high with up to two thirds of the patients showing areas of uterine ischaemia immediately following UAE. In the second part of the study, 86% of the previously reported cases of uterine ischaemia showed complete reversibility and revascularisation at 3 month follow-up MRI. The overall reduction in volume of the ischaemic regions was 98.24% with a reduction of the mean volume of the ischaemic region from 29.29 ml to a mean volume of 0.35 ml after 3 months. The contradiction between the high incidence of occurrence and low incidence of reporting this complication is probably related to the high reversibility of the ischaemia and the ability of the uterine tissue to recover its vascularity. Based on this, it is regarded as a side effect more than a complication.

In all cases with ischaemic changes, the ischaemic regions were variable in size, centrally located and involved both the endometrium and myometrium. The central location of the ischaemic area is probably related to the vascular distribution of the uterine supply with its vessels penetrating the uterus from peripheral to central hence the impact of ischaemia will be most pronounced centrally.

In their meta-analysis, Toor *et al.*[8] grouped uterine infection and uterine ischaemia in one group with an occurrence rate of 0.7% for both entities (26 of 4903 patients). A separate incidence for uterine ischaemia was not given. Another meta-analysis by Martin *et al.*[15] did not report the occurrence of uterine ischaemia in any of the included studies. Their very low incidence reported for uterine ischaemia agrees with our observation of near-complete reversibility of the observed uterine ischaemia.

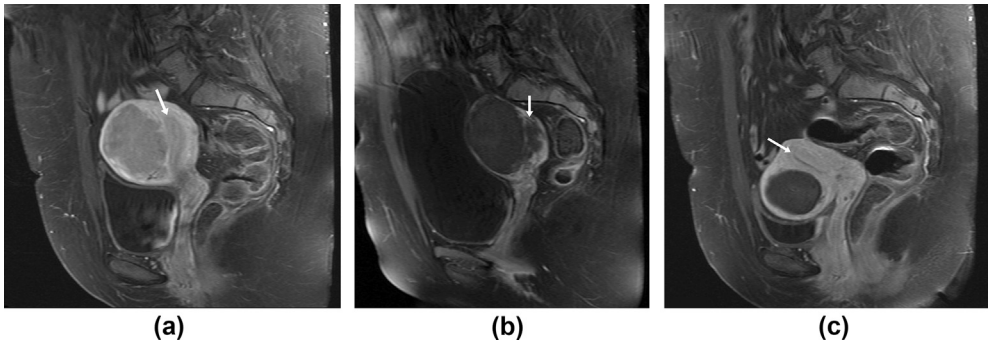


**Figure 2** (a) Pre-embolisation sagittal T1-weighted fat-suppressed MRI of a 46-year-old woman with symptomatic leiomyoma showing an anterior-wall leiomyoma with normal enhancement of the endometrium (white arrow). (b) MRI immediately following embolisation shows a newly developed relatively large area of ischaemia seen as an area of absent enhancement (white arrow) and not corresponding to the location of the uterine leiomyoma (anterior). (c) MRI image after 3 months shows complete revascularisation of the posteriorly located ischaemic area (white arrow) and absent revascularisation of the anteriorly located leiomyoma.

**Table 1**
Measurements of the non-target ischaemic area immediately after uterine artery embolisation (UAE) and change 3 months after UAE in all 29 patients.

| Patient | Age | Ischaemic area | | | | Volume after 3 months | Change in volume (%) |
|---|---|---|---|---|---|---|---|
| | | Length | Width | Height | Volume | | |
| 1 | 47 | 4 | 2.5 | 4.3 | 22.489 | 0.105 | 99.54% ↓ |
| 2 | 38 | 2.9 | 2.1 | 2.5 | 7.963 | 0.000 | 100% ↓ |
| 3 | 46 | 3.1 | 1.8 | 3.4 | 9.922 | 0.000 | 100% ↓ |
| 4 | 46 | 3.7 | 1.9 | 3.9 | 14.339 | 0.000 | 100% ↓ |
| 5 | 55 | 3.4 | 1.8 | 2.3 | 7.362 | 0.000 | 100% ↓ |
| 6 | 46 | 4.7 | 3.3 | 4.1 | 33.258 | 0.000 | 100% ↓ |
| 7 | 45 | 4.4 | 1.4 | 7 | 22.552 | 0.000 | 100% ↓ |
| 8 | 42 | 3.7 | 2.9 | 2.8 | 15.713 | 0.000 | 100% ↓ |
| 9 | 44 | 5.1 | 3.1 | 3.9 | 32.248 | 0.000 | 100% ↓ |
| 10 | 37 | 4.2 | 3.5 | 2.8 | 21.527 | 0.000 | 100% ↓ |
| 11 | 44 | 3.3 | 1.8 | 7.5 | 23.300 | 0.000 | 100% ↓ |
| 12 | 44 | 5.2 | 1.7 | 6.4 | 29.589 | 0.000 | 100% ↓ |
| 13 | 50 | 3.5 | 3.3 | 3.7 | 22.350 | 1.177 | 94.73% ↓ |
| 14 | 49 | 4.5 | 3.6 | 4.2 | 35.585 | 0.000 | 100% ↓ |
| 15 | 42 | 5.8 | 3.9 | 3.1 | 36.674 | 0.000 | 100% ↓ |
| 16 | 44 | 5.5 | 3.9 | 6 | 67.310 | 0.000 | 100% ↓ |
| 17 | 47 | 3.6 | 4.5 | 1.6 | 13.556 | 0.000 | 100% ↓ |
| 18 | 49 | 6 | 5.9 | 2.1 | 38.880 | 0.000 | 100% ↓ |
| 19 | 43 | 3.9 | 2.7 | 3.9 | 21.478 | 0.000 | 100% ↓ |
| 20 | 41 | 2.9 | 1.8 | 4.6 | 12.558 | 3.504 | 72.1% ↓ |
| 21 | 47 | 6 | 4.3 | 6.5 | 87.707 | 0.000 | 100% ↓ |
| 22 | 43 | 2.9 | 2.2 | 4.6 | 15.349 | 0.000 | 100% ↓ |
| 23 | 43 | 3.9 | 3.2 | 3.7 | 24.150 | 0.000 | 100% ↓ |
| 24 | 47 | 2.7 | 2.6 | 3 | 11.014 | 0.000 | 100% ↓ |
| 25 | 54 | 4.8 | 3.9 | 5.2 | 50.911 | 1.883 | 96.3% ↓ |
| 26 | 45 | 5.3 | 1.8 | 6.4 | 31.932 | 0.000 | 100% ↓ |
| 27 | 46 | 6 | 1.4 | 5.7 | 25.041 | 3.400 | 86.42% ↓ |
| 28 | 50 | 4.7 | 4.3 | 5.8 | 61.305 | 0.000 | 100% ↓ |
| 29 | 45 | 5.4 | 4.3 | 4.4 | 53.434 | 0.000 | 100% ↓ |

A single study by Ruuskanen *et al.*[18] discussed the occurrence of uterine ischaemia as a possible prognostic factor for the occurrence of pain. The reported that the incidence of uterine ischaemia was 100%, while the reported mean volume of the ischaemia area was between 35 and 38 ml. The discrepancy in incidence between Ruuskanen *et al.*[18] and the present results is probably attributed to the difference in embolising material used whereby Ruuskanen *et al.*[18] performed embolisation using Embosphere and the present study used Bead Block. The reported mean volume by Ruuskanen *et al.*[18] is close to the present reported volume of ischaemic areas. Scheurig-Muenkler *et al.*[19] performed a similar study on a small number of patients (15 patients) and reported the occurrence of ischaemia in all patients with complete reversibility after short-term follow-up. Again, the reported higher incidence might be attributed to the embolising material used whereby Scheurig-Muenkler *et al.*[19] used Embosphere and the present study used Bead Block. The complete reversibility agrees with the 98.24% reversibility of the ischaemia reported in the present study. Sporadic cases of severe uterine ischaemia with uterine necrosis requiring hysterectomy had been reported.[9,10,20] In such cases the reason for irreversibility of the ischaemic changes are not clear but can be assumed e.g. in one case[20] a very small particle size for embolisation was used (355- to 500-μm PVA) the small size of the embolising material might lead to more aggressive embolisation and hence irreversibility of ischaemia.

Limitations of the present study include the fact that different embolic agents were not compared and that no cases of unilateral embolisation were included to study the incidence when only one side is embolised.

In conclusion, uterine ischaemia following UAE for treatment of uterine leiomyoma is encountered frequently and can be observed in up to two thirds of treated patients. In 86% of cases, the ischaemic regions will disappear at short-term follow-up, and in the remaining patients, the ischaemic regions will be significantly reduced in size.

## Conflict of interest

The authors declare no conflict of interest.

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