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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Possible use of digital variance angiography in uterine fibroid embolization: a retrospective observational study

Viktor Bérczi[1]
Szuzina Fazekas[1]
István Góg[3]
Marcell Gyánó[2]
Ambrus Tóth[1]
Ákos Bérczi[2]
Osama Habeeballah[4]
Krzysztof Pyra[5]
Zoltán Harmat[6]
Dat Tin Nguyen[2]

[1]Semmelweis University, Medical Imaging Center, Department of Radiology, Budapest, Hungary

[2]Semmelweis University, Heart and Vascular Center, Department of Interventional Radiology, Budapest, Hungary

[3]Semmelweis University, Heart and Vascular Center, Department of Vascular and Endovascular Surgery, Budapest, Hungary

[4]University Hospital Augsburg, University of Augsburg, Department of Diagnostic and Interventional Radiology, Augsburg, Germany

[5]Medical University of Lublin, Department of Interventional Radiology and Neuroradiology, Lublin, Poland

[6]Premier Med Healthcare, Training and Research Institute, Budapest, Hungary

PURPOSE

Digital variance angiography (DVA), a recently developed image processing technology, provides a higher contrast-to-noise ratio (CNR) and better image quality during lower limb interventions than digital subtraction angiography (DSA). Our aim was to investigate whether the quality reserve of DVA can also be observed in uterine fibroid embolization (UFE).

METHODS

In this retrospective observational study, the CNR and image quality of DSA and DVA images from 56 patients (mean ± standard deviation age: 44.2 ± 5.3 years) who underwent UFE at our institution were assessed. For the visual evaluation of the same image pairs, the visibility of large vessels, small vessels, tissue blush, and background noise was compared by three experienced readers using a four-grade Likert scale. Data were analyzed using the Wilcoxon signed-rank test or the one-sample Wilcoxon test.

RESULTS

DVA provided significantly higher CNR than DSA (the median CNR_{DVA}/CNR_{DSA} was 1.96). In the visual comparison of DVA and DSA images, Likert scores did not significantly differ from zero (equal quality level) in any evaluated categories. The median (interquartile range) values were 0.00 (1.00) for large vessels, −0.33 (1.33) for small vessels, 0.00 (0.67) for tissue blush, and 0.00 (0.75) for background noise.

CONCLUSION

Although the visual image quality of DSA and DVA was identical, DVA provided a twofold CNR in UFE, indicating a significant quality advantage for this technology.

CLINICAL SIGNIFICANCE

The observed quality reserve may allow for dose management (reduction of applied radiation dose and/or contrast media), enhancing the safety of UFE for both patients and personnel.

KEYWORDS

Angiography, contrast-to-noise, digital, uterine, uterine fibroid embolization

Corresponding author: Viktor Bérczi

E-mail: berczi.viktor@semmelweis.hu

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Digital variance angiography (DVA) is a recently developed image processing alternative to digital subtraction angiography (DSA). The technology is based on the principles of kinetic imaging.[1] Although DVA uses the same unsubtracted acquisition as DSA, it does not use a mask but instead calculates the standard deviation (SD) of pixel intensities. This algorithm enhances the contrast media signal and suppresses background noise, thereby providing a higher contrast-to-noise ratio (CNR) and better image quality than DSA. The quality reserve of DVA has already been validated in lower limb angiography,[2-5] liver transarterial chemoembolization,[6] prostatic artery embolization,[7] and carotid angiography.[8] As the quality advantage of DVA can be effectively used for dose management,[8-10] the aim of this study was to investigate whether DVA can improve the image quality of angiograms in transcatheter

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uterine fibroid embolization (UFE), which could serve as a basis for radiation dose management in this endovascular intervention.

Over the last 29 years, as stated in the 2015 CIRSE guideline, numerous publications have demonstrated that UFE is a viable alternative to hysterectomy for women who wish to preserve their uterus (level 1 evidence).[11-14] The 2021 ACOG guideline confirms these findings, stating that "uterine artery embolization (UAE) is recommended as an interventional procedure for the treatment of uterine leiomyomas in patients who desire uterine preservation and are counseled about the limited available data on reproductive outcomes".[15] In addition to fibroids, UAE has also been proposed as a minimally invasive alternative to hysterectomy for patients with symptomatic adenomyosis.[16,17]

UAE is much less invasive and a non-surgical alternative to myomectomy or hysterectomy; however, ionizing radiation is used to identify and access the uterine artery for the embolization procedure. The literature shows that radiation exposure doses remain below the threshold for any deterministic radiation risks. Despite these data, implementing the ALARA principle and minimizing the radiation dose as much as possible is of utmost importance in every interventional radiological procedure, especially in UAE, as many patients are women of child-bearing age. Many papers have discussed different dose reduction techniques, such as adjusting collimation, minimizing DSA runs, reducing frame rates, using PA projections, and employing dose optimization software.[18,19] The use of DVA has not yet been tested in UFE.

Main points

- Use of digital variance angiography (DVA) in uterine fibroid embolization (UFE): the study evaluates DVA as an alternative to traditional digital subtraction angiography (DSA) in UFE.
- Enhanced contrast-to-noise ratio (CNR): findings demonstrate that DVA offers a twofold higher CNR compared with DSA, indicating a substantial quality reserve.
- Potential for dose management: with the higher CNR provided by DVA, there is potential to reduce radiation exposure without compromising image quality, which is particularly advantageous for women of childbearing age.
- Implications for future clinical trials: the study suggests that future prospective clinical trials should focus on validating the dose management capabilities of DVA in endovascular treatments, with the potential to reduce radiation exposure for both patients and personnel.

Methods

In this single-center retrospective observational study, 56 patients (mean ± SD age: 44.2 ± 5.3 years) were included who had previously undergone UFE at the Medical Imaging Center, Semmelweis University, Budapest, Hungary, between February 2021 and June 2022. All procedures were conducted in accordance with the 1964 Helsinki Declaration and its later amendments. The study was approved by the Regional Institutional Scientific and Research Ethics Committee, Semmelweis University, Budapest, Hungary (SE RKEB), approval no. 186/2022 on September 26, 2022. Due to the retrospective nature of the study, informed consent was waived.

Study Design

One pre-embolization posteroanterior (PA) pelvic acquisition was included from each patient. Pre-embolization acquisition was preferred as it depicts small arteries and tissue blush of the fibroid, thereby providing a better basis for performance comparison. DSA and DVA images were generated retrospectively from the same unsubtracted acquisition using the GE Advantage Workstation (GE Healthcare, Chicago, Ill., U.S.A.) and the Kinepict Medical Imaging Tool software (Kinepict Ltd., Budapest), respectively. Absolute CNR values and ratios were calculated for each image pair, and visual image quality was assessed by readers in a blinded and randomized manner using a 4-grade Likert scale.

Image acquisition

All procedures followed institutional protocols. UFE was performed on a GE Innova IGS 5 angiography system by an experienced interventional radiologist with over 20 years of experience. A 4F UF (Cordis, Miami Lakes, FL, U.S.A.) catheter was introduced via right femoral access. Aortography was performed to assess arterial filling of the fibroids. A Medrad Avanta (Bayer AG, Leverkusen, Germany) automated injector was used to inject 20 mL of iodinated contrast media (Ultravist 370, Bayer) at a flow rate of 10 mL/s. A 4F Cobra 1 Glidecath (Terumo, Leuven, Belgium) was positioned in the left uterine artery, followed by the right uterine artery. Hand injections of contrast media (3–6 mL) were performed for the selective angiograms into the uterine arteries. Standard PA pelvic acquisitions (2 fps) were obtained on both sides before and after embolization. DSA runs were saved on the GE workstation, and the unsubtracted files were later used to generate stacked DSA and DVA images as described above.

Contrast-to-noise ratio analysis

Regions of interest (ROIs) were defined on vessels and background regions using ImageJ (v.2.0.0-rc-68/1.52e, Creative Commons License, NIH). As adjacent regions of blood vessels often contained signals from small arteries or tumor blush, background ROIs were placed outside the fibroid area. Vascular and background ROIs were paired accordingly.

The CNR values were calculated for all ROI pairs individually using the following formula [21], where $Mean_v$ and $Mean_b$ represent the mean pixel intensity values of the vascular and background ROIs, respectively, and Std_b is the background SD:

$$CNR = \frac{|Mean_v - Mean_b|}{Std_b}$$

CNRDVA/CNRDSA ratios (R) were also calculated for each corresponding DVA and DSA ROI.

Visual evaluation

Evaluations were conducted by three interventional radiologists with at least 5 years of experience in UFE. The readers were not involved in the treatment of enrolled patients.

A randomized, paired evaluation was performed with corresponding DSA and DVA image pairs. The readers were blinded to the imaging modality. The diagnostic value of the acquisitions was compared based on the visibility of large vessels, small vessels, tissue blush (if visible), and the extent of background noise (Figure 1).

Diagnostic value was graded using the following 4-grade bidirectional Likert scale:

0. Identical

1. Slightly better/less noise

2. Clear-cut advantage/less noise, no interference with structures

3. Better in every aspect/less noise, no interference, background clear

Each image pair was evaluated only once during the survey, and scores were automatically collected in a database for later processing.

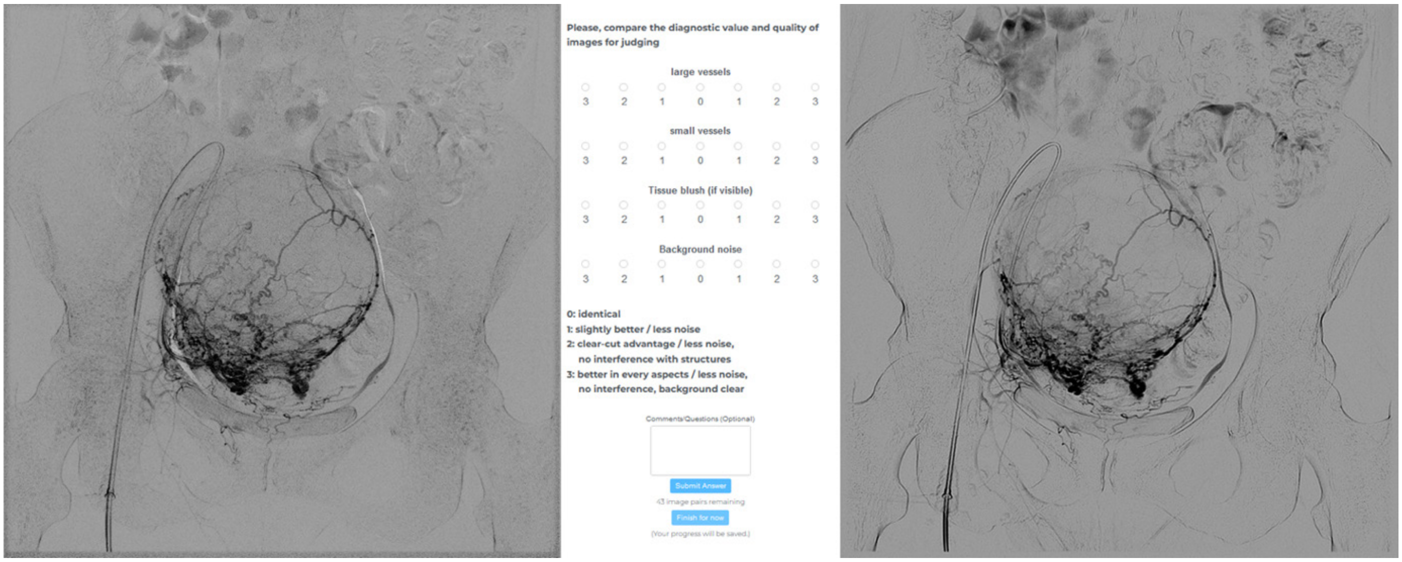

Figure 1. Survey template for the visual evaluation of DSA and DVA image sets. The modality of images was not disclosed to the readers. The web-based survey allowed for the automatic collection of scores into a database for later processing. DSA, digital subtraction angiography; DVA, digital variance angiography.

Table 1. Contrast-to-noise ratio (CNR) analysis

	CNR		R	Wilcoxon signed-rank test
	DSA	DVA	CNR_{DVA}/CNR_{DSA}	DSA vs. DVA
Mean ± SEM	19.2 ± 0.55	33.4 ± 0.73	2.01 ± 0.04	$P < 0.001$
Median (IQR)	16.2 (13.24)	29.6 (24.96)	1.96 (0.88)	

Data are expressed as mean ± standard error of the mean (SEM) and median and interquartile range (IQR). The Wilcoxon signed-rank test was used for statistical comparison, with a significance level set at $P < 0.05$. DVA, digital variance angiography; DSA, digital subtraction angiography.

Radiation dose and total fluoroscopy time measurements

Radiation dose (total dose-area product - DAP) and total fluoroscopy time were gathered from the radiation dose information provided for each patient in the "X-ray Radiation Dose Report" of the GE Innova IGS 5 angiography system. Data are presented as median (interquartile range).

Statistical analysis

Calculations of CNR and R medians, along with interquartile ranges (IQR), were performed using Excel 2016 (Microsoft, Redmond, WA). CNR values were compared using the Wilcoxon signed-rank test (Prism 8.4.2, GraphPad).

For visual evaluation scores, the mean and standard error of the mean were calculated. Due to the non-Gaussian distribution of the data, the median and IQR were also determined. To assess potential differences between modalities, image pair scores were compared with 0 (equal quality level) using the one-sample Wilcoxon test. Interrater agreement was characterized by Kendall's W value. The level of significance was set at $P < 0.05$ for all tests.

Results

Patients

Patients (n = 56, mean ± SD age: 44.2 ± 5.3 years) with previously diagnosed uterine fibroids received UFE treatment between February 2021 and June 2022 at the Medical Imaging Center, Semmelweis University, Budapest, and were retrospectively enrolled for image analysis in a consecutive manner.

Contrast-to-noise ratio results

A total of 695 ROI pairs were analyzed from 56 pre-embolization image pairs. The results of the CNR measurements are summarized in Table 1. The median CNR of DVA images was significantly higher than that of DSA images [29.55 (IQR: 24.96) vs. 16.23 (IQR: 13.24), Wilcoxon signed-rank test, $P < 0.001$). The R (CNRDVA/CNRDSA) value was 1.96 (IQR: 0.88) (Figure 2).

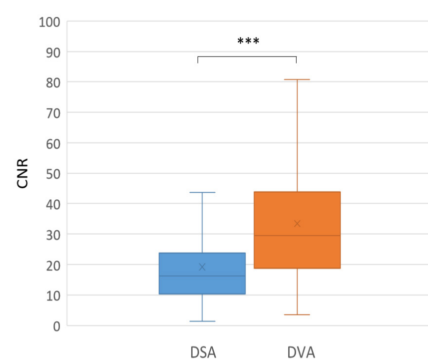

Figure 2. The CNR results. The box-and-whisker plots show the median (line), mean (x), IQR (box), and internal fences (whiskers) of CNR values in each group. Data sets were analyzed using the Wilcoxon signed-rank test (*$P < 0.001$). CNR, contrast-to-noise ratio; IQR, interquartile range; DSA, digital subtraction angiography; DVA, digital variance angiography.

Visual evaluation results

Readers evaluated 56 DSA-DVA image pairs using the 4-grade bidirectional Likert scale, where 0 represented identical image quality. According to the score settings, negative values indicated an advantage for DSA, whereas positive values indicated an advantage for DVA (Table 2). The median (IQR) Likert scores were 0.00 (1.00) for large vessels, −0.33 (1.33) for small vessels, 0.00 (0.67) for tissue blush, and 0.00 (0.75) for background noise (Figure 3). None of these values were significantly different from zero (one-sample Wilcoxon test).

Table 2. Visual comparison scores. Readers compared the visibility of large vessels, small vessels, tissue blush, and the level of background noise in a blinded, randomized manner, expressing their image preference using a 4-grade Likert scale

	Large vessels	Small vessels	Tissue blush	Background noise
Mean ± SEM	0.11 ± 0.11	−0.24 ± 0.14	0.10 ± 0.07	0.01 ± 0.10
Median (IQR)	0.00 (1.00)	−0.33 (1.33)	0.00 (0.67)	0.00 (0.75)
One-sample Wilcoxon test	$P = 0.355$	$P = 0.054$	$P = 0.151$	$P = 0.98$

Data are expressed as mean ± SEM and median and IQR. Deviation from zero (equal quality level) was analyzed using the one-sample Wilcoxon test. None of the scores differed significantly from zero. SEM, standard error of the mean; IQR, interquartile range.

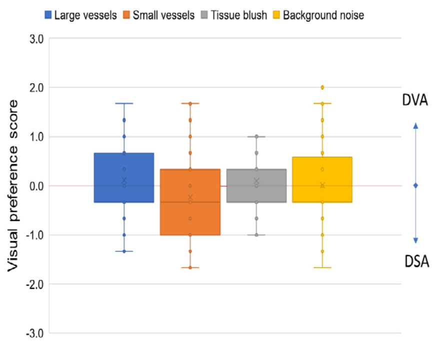

Figure 3. Paired comparison of DSA and DVA images. Readers compared the visibility of large vessels, small vessels, tissue blush, and background noise in a blinded, randomized manner, expressing their preference using a 4-grade Likert scale. The box-and-whisker plot displays the mean (x), median (line), interquartile range (box), and internal fences (whiskers) of the complete image set. The 0 line represents the theoretical equal quality level. Data were analyzed using the one-sample Wilcoxon test. None of the scores differed significantly from zero. DSA, digital subtraction angiography; DVA, digital variance angiography.

Despite moderate interrater agreement levels, ratings were significantly associated with large vessels ($W = 0.568$, $P < 0.001$) and small vessels ($W = 0.502$, $P < 0.01$). However, agreement was only slight and not significant for tissue blush ($W = 0.285$, $P = 0.766$) and background noise ($W = 0.349$, $P = 0.378$).

Radiation dose and total fluoroscopy time

Total DAP was 57.0 (21–284) Gy·cm^2, and total fluoroscopy time was 736 (360–1570) sec.

Discussion

Our aim was to investigate whether the previously described advantages of DVA can also be observed in UFE intervention. Therefore, we compared the CNR and visual performance of DSA and DVA images in this retrospective observational study. Our results show that DVA provides a significantly higher (about twofold) CNR than DSA, but there is no difference in the visibility of large vessels, small vessels, tissue blush, and background noise. The poor interrater agreement in the latter two categories might reflect that the judgment of tissue blush and background noise is even more subjective. These findings are partly inconsistent with previous observations, as earlier studies demonstrated that DVA was always superior to DSA in both parameters.[2-10] However, in the present study, angiography conditions were different, as the catheter was in the uterine artery, very close to the target area, ensuring a highly selective injection of contrast media, and the acquisition was performed at a standard radiation level. Under these conditions, DSA provides excellent visual representation, which cannot be outperformed (ceiling effect). Nevertheless, the improved CNR value clearly indicates the quality reserve of DVA.

Previous studies have demonstrated that the quality reserve of DVA can be effectively utilized for dose management. A reduction of dose/frame value by 70% provided non-inferior or superior image quality in lower limb interventions compared with full-dose DSA acquisitions.[20] A subsequent randomized controlled trial showed that applying a similar low-dose protocol reduced total DSA-related DAP by 63% and total procedural DAP by 46% without compromising image quality or the diagnostic value of angiograms.[21] The quality reserve of DVA can also be used to reduce contrast media, as DVA provided non-inferior image quality in carotid angiography compared with full-dose DSA when only 50% of the contrast media amount was used.[8] Our preliminary unpublished observation suggests that an 80% reduction in contrast media achieved through dilution still provides excellent image quality in UFE using DVA images, whereas the concomitant DSA images under the same conditions appear poor.

Our finding may have important clinical implications if further studies prove the relevance of the increased CNR and increased quality reserve. UFE is a good alternative for the treatment of uterine fibroids, as it presents less burden and less risk for patients than surgical solutions. Nevertheless, this endovascular intervention requires several X-ray angiography acquisitions and repeated injections of iodinated contrast media. These steps carry their own risks, including possible acute and long-term side effects of radiation and potential impairment of kidney function. Obviously, the dose management capabilities, especially the radiation dose reduction ability of DVA, could be very beneficial in UFE, as patients are often of reproductive age. In addition, lower radiation exposure would reduce the risk of radiation-induced occupational hazards for medical staff. The reduction of contrast media usage could also be advantageous by lowering the risk of contrast-induced nephropathy.

Our results reveal the potential of DVA for dose management in UFE; nevertheless, further clinical studies are required to validate these claims. Such a study has already been initiated at our center. The radiation dose from our center serves as a baseline for such a study; our data fall well within the range of recent literature [DAP (Gy·cm^2; median, range): Nocum et al.[22]: 113.1 (21.9–792); Lacayo et al.[23]: 74.8 (0.32–795); our data: 57 (21–284); total fluoroscopy time (minutes, median, range): Nocum et al.[22]: 11.1 (6.2–33.6); Lacayo et al.[23]: 13.5 (5.7–104); our data: 12.2 (6.0–26.2)].

Our study has some limitations. Due to its retrospective observational nature, the acquisition protocol was predefined and optimized for DSA; therefore, we could not detect any differences in the visual performance of DSA and DVA images. The full validation of DVA in UFE requires prospective clinical trials in which the protocol is appropriately modified to achieve dose management and DVA images are available for the interventional radiologist in real-time in the operating room.[24]

In conclusion, our data show that DVA has a substantial quality reserve in uterine artery angiography compared with the traditionally used DSA technology. Although a visual advantage was not observed in the current clinical setting, the twofold CNR of DVA images provides a solid basis for prospective clinical trials, where the dose management capabilities of DVA can be validated in the endovascular treatment of fibroids and adenomyosis. These trials aim to achieve a 70% reduction in dose/frame value while maintaining non-inferior or superior image quality, as already demonstrated in lower limb interventions. Thus, our study indicates that DVA has the potential to reduce the applied radiation dose during UFE for both patients and personnel.

Footnotes

Conflict of Interest

The authors declared no conflicts of interest.

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