Application of kinetic imaging in catheter angiography - comparison of digital variance angiography (DVA) with digital subtraction angiography (DSA)

Ph.D. thesis

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1. INTRODUCTION

Atherosclerotic vascular diseases are one of the leading causes of death in Hungary. The condition is a generalized disease, however, manifestation and severity may vary in different vascular areas. In Hungarian prevention programs, the recognition and the treatment is focused on the coronary and brain artery lesions, while the symptomes of peripherial arterial disease (PAD) are often recognized late and inadequately.

The methods that are used in the diagnosis of different vascular areas shows significant similarities. Non-invasive ultrasound, computed tomography (CT), magnetic resonance (MR) imaging can be used with good results in each region. Catheter angiography is not only a diagnostic tool, it also provides a therapeutic option even in a single session.

The theoretical bases of catheter angiography were described in 1896, the year after the discovery of X-ray, but they were only applied in clinical settings from the 1920s. Nevertheless, compared to the other methods, this method has the most significant history and, thanks to its continuous development, it is an opportunity for therapeutic purposes also in a single session. With the technique described by Seldinger and the vasodilatory possibilities provided by balloons and stents, despite the fact that it uses ionizing radiation, it is expected to remain one of our most important tools in the treatment of vascular diseases for a long time.

Digital variance angiography (DVA) is a new method, that was described by Krisztián Szigeti and Szabolcs Osváth, who are researchers of the Department of Biophysics and Radiation Biology of Semmelweis University. DVA is calculated from the variance of X-ray absorption in time. Based on the theoretical description of the method, it can be assumed that the new technology also enables better image quality and / or radiation dose reduction.

2. OBJECTIVES

- In the first step, we wanted to investigate the phisical and diagnostical/clinical image quality of DSA and DVA lower limb angiography images.

With retrospective analysis of standard lower limb angiography series with DSA-specific settings:

1. Is the signal-to-noise ratio of DVA images better than DSA?

2. Is the clinical/diagnostical image quality of DVA images better than DSA?

- In the second step, we planned to clarify wether the quality reserve of DVA images can be used for radiation dose reduction.

By comparing the DSA and DVA images of full and reduced radiation dose lower limb angiography images:

3. How does the signal-to-noise ratio change for radiation dose reduction?

4. How does the diagnostic usability of a reduced-dose DVA image compare to a full-dose, daily routine DSA image?

3. METHODS

3.1. First study: retrospective analysis of standard clinical care diagnostic angiography images with DSA and DVA method

3.1.1. Study design

The study was performed of the license of National Institute of Pharmacy and Nutrition of Hungary (n.2830/2017) in the Catheter Laboratory of the Heart and Vascular Center. 42 patients were included. All examinations were elective case, followed by standard clinical protocol, indicated by vascular surgeons. We made the raw and the postprocessed DVA images with Kinepict software and summation DSA images with Fiji software. We used too the standard DSA images in the visual comparison to evaluate the diagnostic image quality of both method. (Figure 1).

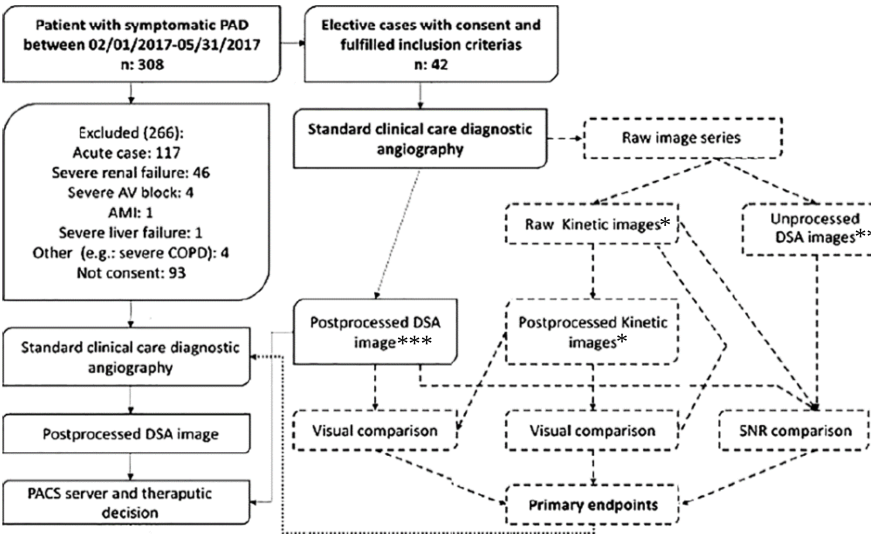


Fig. 1. Flowchart of the study: the solid lines represent the daily routine of lower limb angiography, while the sections marked with a dashed line show a specific part of the study. * Kinepict software, ** Fiji software, *** Siemens Syngo software.

3.1.2. Analysis of the signal-to-noise ratio

Signal-to-noise ratio (SNR) is a physical parameter that characterizes the quality of the images well. The SNR values were analysed according to the Rose method. Signal intensity was calculated from the visually perceptible vessels and from the nearly non-vascular regions with an average size area of 100 pixels. Measurements were also performed on raw DVA, summation and postprocessed DSA images in the abdominal, pelvic, and femoral regions. In the more distal regions, we did not perform any measurements due to the fact that the commonly used side-selective postprocessing (e.g., pixel-shift) influenced the signal intensity.

3.1.3. Diagnostic image quality

We compared raw and postprocessed DVA images with an online blind test, and postprocessed DVA and standard clinical DSA images in another questionnaire. Each questionnaire was completed by three vascular surgeons and three radiologists. We asked three questions:

1. Which image is more detailed?
2. In which image are anatomic structures more discernible?
3. Which image is more useful diagnostically?

3.1.4. Statistical analysis

The median SNR values of an image type were compared to each other. Responses to diagnostic quality were also analyzed in aggregate and by region. After establishing the 95% confidence interval, we examined the interrater agreement by giving the percentage of agreement with the K (kappa) function of the Stata 15.0 (StataCorp, College Station, USA) program, and then performed a Fleiss K test to determine the significance of the agreement level.

3.2 Second study: evaluation of 100% and 30% radiation dose lower limb angiography images with DSA and DVA technology in the abdominal, femoral and crural regions

3.2.1. Study design

The study was performed of the same license in the same location like the first one. Thirty patients were included in the study. Patients arrived for lower extremity angiography indicated by vascular surgeons. All examinations were elective case. All patients had normal renal function. We recorded duplicated series of the abdominal, femoral, and proximal crural region with reduced (0.36 microGy / frame) and normal (1.20 microGy / frame) dosage. Any other settings were the same in both acquisiton. We made the postprocessed DSA and DVA images from each acqusition. (Figure 2)

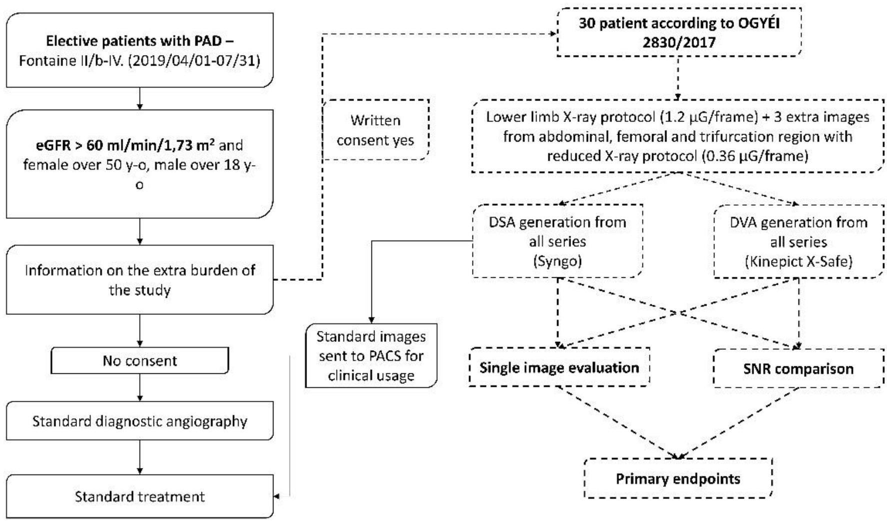


Fig. 2. Flowchart of the study: solid lines represent the daily routine of lower limb angiography, while the sections marked with a dashed line show a specific part of the study. Software types is shown in parentheses.

3.2.2. Investigation of the reached dose reduction

The extent of the planned 70% radiation dose reduction was analyzed from the dose reports associated with the recordings as the value of the dose area product (DAP, microGy/cm^2) that correlated with the number of frames.

3.2.3. Analysis of the signal-to-noise ratio

The signal-to-noise ratio was examined according to Rose Signal intensity was calculated from the visually perceptible vessels and from the nearly non-vascular regions with an average size area of 100 pixels. Measurements were performed on all types of images in the abdominal and femoral region. In the proximal crural region measurement was not performed due to the fact that commonly used side-selective postprocessing (e.g., pixel-shift) affects signal intensity.

3.2.4. Diagnostic image quality

Using an online blind test, each image was rated separately with a Likert scale of 1 to 5. Value 4 corresponded to the daily routine image quality. The questionnaire was completed by three vascular surgeons and four interventional radiologists.

3.2.5. Statistical analysis

The quotient of the median SNR values was examined for each image type.

To examine the diagnostic quality of the images, the mean and standard deviation values and the median of the Likert scale scores were analyzed, and then the significance level of the differences between the image types was quantified by Wilcoxon signed rank test. Grubbs test was performed to outlier detection. Each test was performed using the Stata 15.0 program (StataCorp, College Station, USA).

4. RESULTS

4.1. First study: retrospective analysis of standard clinical care diagnostic angiography images with DSA and DVA method

4.1.1. Signal-to-noise ratio

A total of 1902 area pairs were measured, 817 in the abdominal region, 396 in the pelvic region, and 689 in the femoral region. The DVA SNR values were higher in every case than DSA. Raw DVA SNR values were higher 2.1–2.4-fold than the postprocessed DSA SNR values.

4.1.2. Diagnostic image quality

In the case of the questionnaire where the post-processed DSA image was also included, we observed a tendentious response of one of the respondents, therefore in both questionnaires we performed the evaluation for 5 and 6 respondents as well.

When comparing raw and post-processed DVA images, in 6 evaluators, out of 4176 answers to all questions, the post-processed image was preferred in 2668 cases (63.9%). The agreement between the respondents was 75% for all image pairs examined ($p < 0.001$ for all three questions).

In the case of 5 evaluators, the result did not change significantly: out of 3480 answers to all questions, the post-processed image was preferred in 2345 cases (67.4%). The agreement between the respondents was 79% ($p < 0.001$).

When comparing postprocessed DVA and postprocessed DSA images, taking into account all evaluators and all responses, out of 4284 responses, the postprocessed DVA image was judged to be better in 2607 cases (60.8%). The agreement between the respondents was 74% ($p < 0.001$).

For 5 evaluators, out of 3570 responses, the postprocessed DVA image was selected over the postprocessed DSA in 2462 cases. This corresponds to 69.0%, a significant increase from the previous 60.8%. The agreement between the respondents increased to 81% ($p < 0.001$).

According to the opinion of the outlier the bony edge appearing as a smoother line in the DVA images, that caused the preference of DSA.

By region, DVA was preferred in the areas containing smaller vessels, which was most pronounced in the popliteal and talocrural areas. Here, there was significant agreement among the evaluators that the postprocessed DVA image is better than the one with paired it.

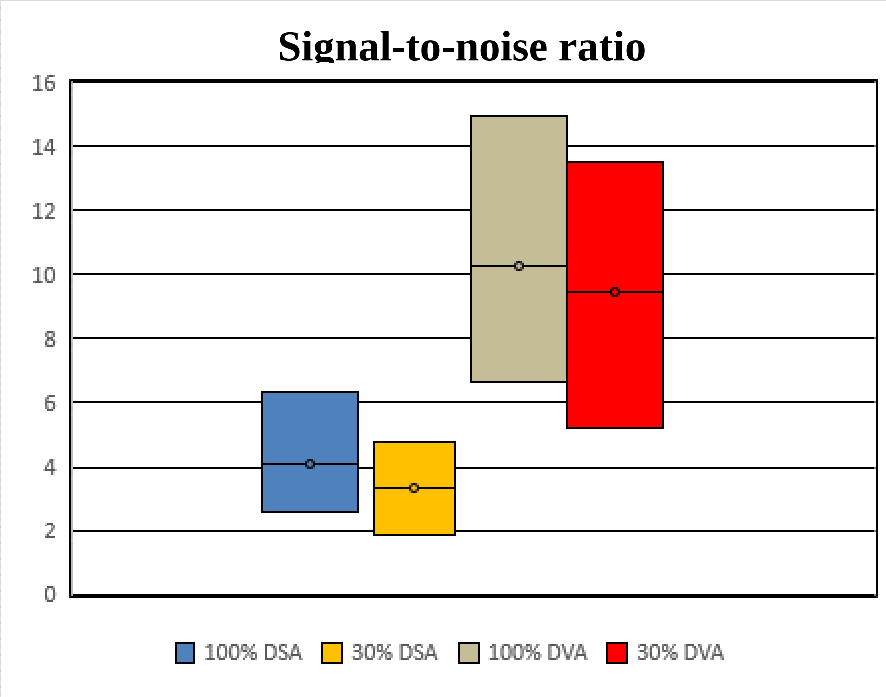
4.2. Second study: evaluation of 100% and 30% radiation dose lower limb angiography images with DSA and DVA technology in the abdominal, femoral and crural regions

4.2.1. Investigation of the reached dose reduction

Based on the DAP values correlated with the number of frames, the reduced-dose images were taken with an average radiation dose of 29-33% per frame, which corresponds to the planned one.

4.2.2. Signal-to-noise ratio

19198 measurements were used for the statistical analysis, based on the median SNR of 30% reduced-dose DVA and full-dose DSA images. The ratio of the median SNR values was 2.06 (1.48-2.87). According this, the SNR of the reduced radiation dose DVA image exceeded the SNR of the 100% DSA image. (Figure 3)



SNR	100% DSA	30% DSA	100% DVA	30% DVA
Median	4,07	3,33	10,25	9,45
Q1	2,62	1,83	6,68	5,22
Q3	6,32	4,77	14,96	13,52

Figure 3. Signal-to-noise ratios (SNR) of the images. It can be seen that the SNR of DSA values are lower than SNR of DVA with both radiation dose level. DVA had larger standard deviation, which indicates the sensitivity of the method.

4.2.3. Diagnostic image quality

There were 30–30 image pairs in the abdominal and femoral regions, and a total of 58 image pairs in the crural region due to side-selective postprocessing. A total of 472 images were evaluated by all (7) evaluators, for a total of 3304 responses, representing 826 ratings per image type. A Grubbs test was performed, but only one outlier was detected in the femoral region who tended to prefer DSA regardless of radiation dose. Therefore we also performed statistical evaluation with 6 and 7 evaluators in this region using the Wilcoxon signed rank test.

Comparison of scores for full-dose DSA images and reduced-dose DVA images in the abdominal region showed no significant difference (3.49 vs 3.23, number of image pairs: 30, number of responses received 420, $p > 0.05$). (Table 1, Figure 4)

Table 1. Scores in the abdominal region. (R - reduced dose image, E - full dose image)

Abdominal	DSA R	DSA E	DVA R	DVA E
Mean	2,99	3,49	3,23	3,67
St. dev.	0,73	0,78	0,83	0,80
Median	3	4	3	4

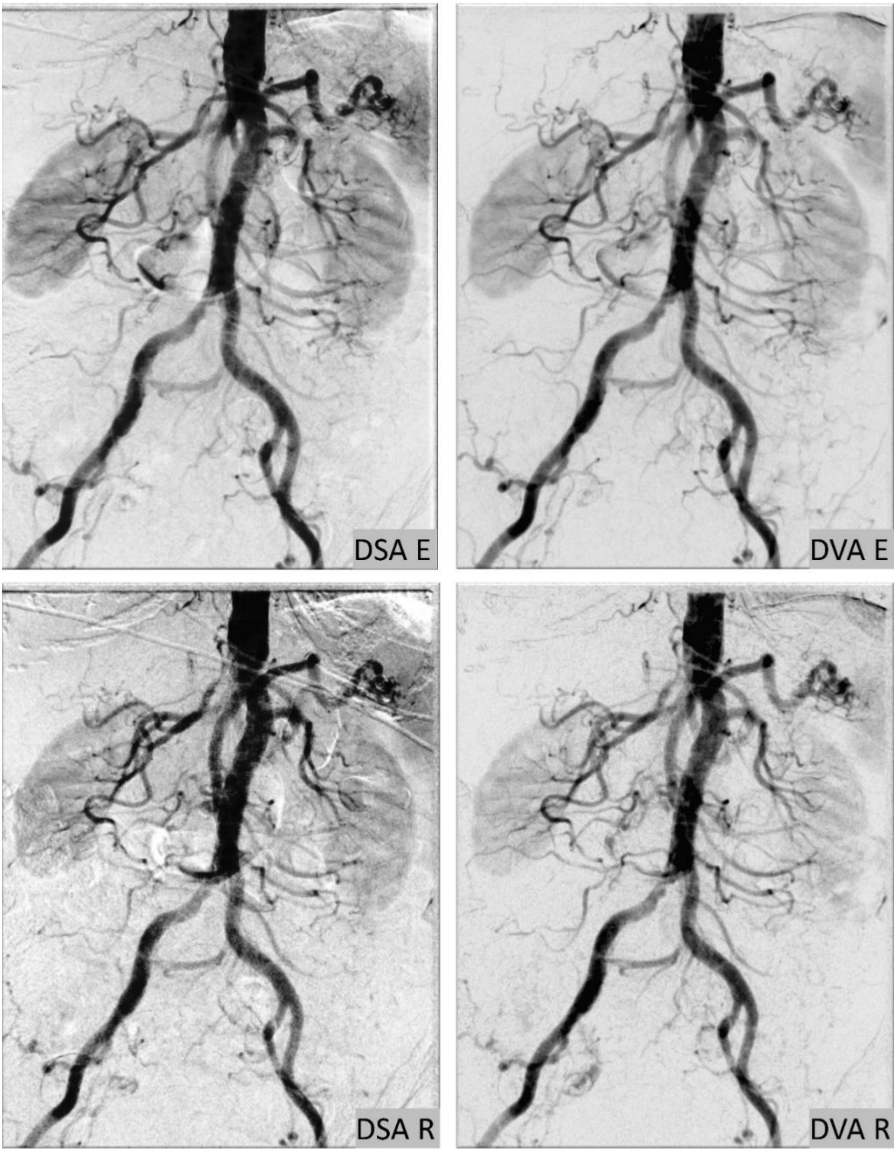


Figure 4. Full (E) and reduced (R) radiation dose images of the abdominal region according to the indexed methods.

In the femoral region, the comparison of scores for full-dose DSA images and reduced-dose DVA images showed a significant difference (4.28 vs 4.10, number of image pairs: 30, number of responses received 420, p <0.05) in 7 respondents. Excluding the outlier significantly altered the result: the scores of full-dose DSA images did not change significantly (4.28 vs 4.27), while the scores of reduced-dose DVA images increased (4.10 vs. 4.19). Performing the Wilcoxon test in this way, we found no significant difference (4.27 vs 4.19, number of image pairs: 30, number of responses received 360, p> 0.05). (Table 2, Figure 5)

Table 2. Scores in the femoral region. (R - reduced dose image, E - full dose image)

7 rater	DSA R	DSA E	DVA R	DVA E
Mean	4,07	4,28	4,10	4,22
St. dev.	0,78	0,67	0,73	0,65
Median	4	4	4	4
6 rater	DSA R	DSA E	DVA R	DVA E
Mean	4,07	4,27	4,19	4,32
St. dev.	0,78	0,67	0,69	0,58
Median	4	4	4	4

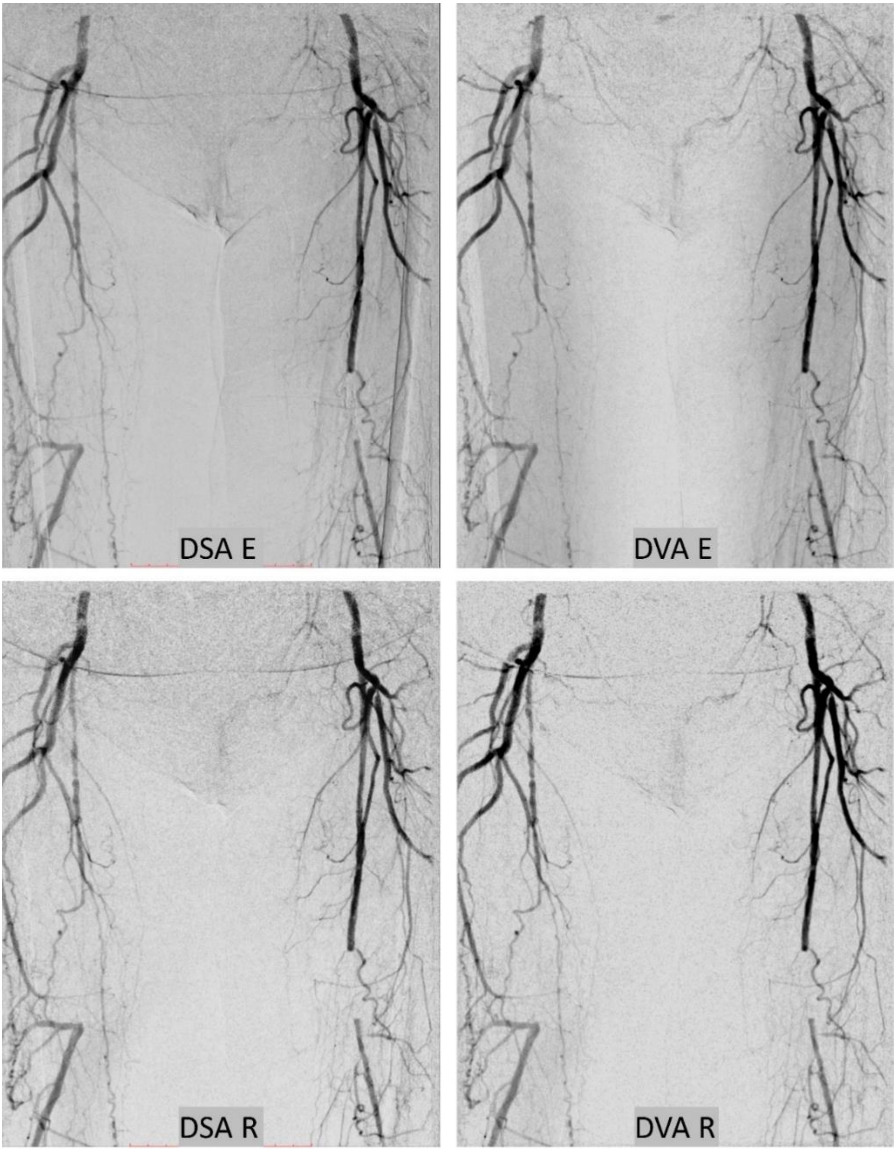


Figure 5. Full (E) and reduced (R) radiation dose images of the femoral region according to the indexed methods.

In the crural region, comparison of scores for full-dose DSA images and reduced-dose DVA images showed a significant difference (3.37 vs 3.62, number of image pairs: 58, number of responses received 812, $p < 0.05$). (Table 3, Figure 6)

Table 3. Scores in the crural region. (R - reduced dose image, E - full dose image)

Crural	DSA R	DSA E	DVA R	DVA E
Mean	3,14	3,37	3,62	3,99
St. dev.	0,91	0,83	0,91	0,84
Median	3	3	4	4

We examined the total scores for all regions (including the outlier), the comparison of scores for full-dose DSA images and reduced-dose DVA images showed no significant difference (3.63 vs 3.64, number of image pairs: 118, number of responses received 1652, $p > 0.05$). (Table 4)

Table 4 Scores in all regions with all evaluators. (R - reduced dose image, E - full dose image)

	DSA R	DSA E	DVA R	DVA E
Mean	3,34	3,63	3,64	3,96
St. dev.	0,94	0,87	0,90	0,81
Median	3	4	4	4

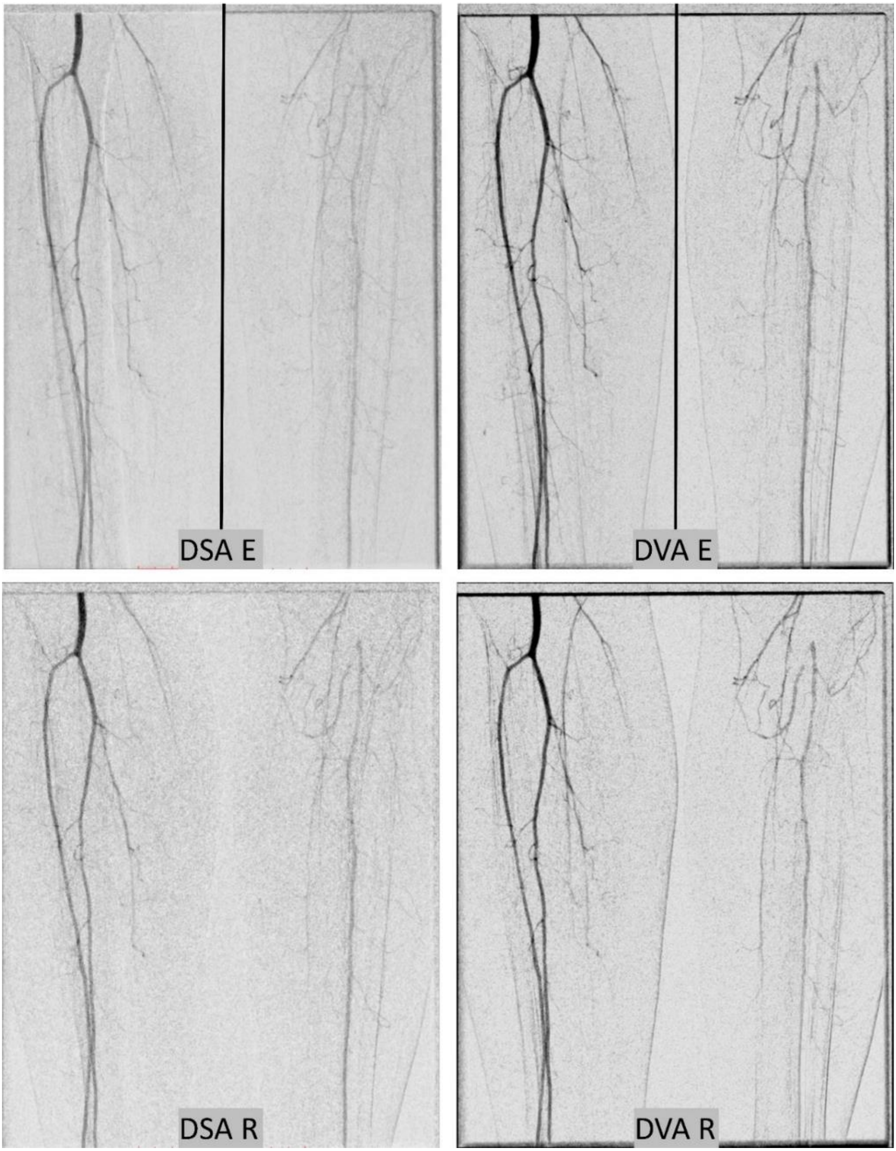


Figure 6. Full (E) and reduced (R) radiation dose images of the crural region according to the indexed methods.

5. CONCLUSIONS

Based on our two studies, we can conclude:

- In a retrospective analysis of standard clinical care diagnostic angiography images with DSA and DVA method

1. DVA images showed 2.1-2.4 times better signal-to-noise ratio compared to DSA images.

2. Post-processed DVA images diagnostic value were 69% better to compared the daily routine post-processed DSA images with the level of 81% interrater agreement.

- By comparing the image quality of full radiaton dose DSA and reduced dose DVA images:

1. With 70% radiation dose reduction, the signal-to-noise ratio of DVA images exceeded the signal-to-noise value of full-dose DSA images. The median of the DVA / DSA signal-to-noise ratio was 2.06.

2. With 70% dose reduction, the mean Likert points for DVA images were 3.64, while the full-dose DSA images score was 3.63.

Limitations

1. We performed the comparison only in a well-defined regions, while the DSA method can be used in several other regions (e.g. carotid system).

2. The standard DSA images were always available under reduced-dose acquisitions, so the usability of the reduced-dose DVA image alone requires further investigation.

6. PUBLICATIONS

International publications used for the dissertation:

1. **M. Gyánó**, I. Góg, V.I. Óriás, Z. Ruzsa, B. Nemes, C. Csobay-Novák, Z. Oláh, Z. Nagy, B. Merkely, K. Szigeti, S. Osváth, P. Sótonyi: Kinetic Imaging in Lower Extremity Arteriography: Comparison to Digital Subtraction Angiography. Radiology. 2019 Jan; 290(1):246-253. **IF: 7,608**

2. **M. Gyánó**, K. Szigeti, S. Osváth, J. Kiss, C. Csobay-Novák, B. Nemes.: Dose management capability of digital variance angiography (DVA): a 70% reduction of radiation dose in lower limb angiography. ECR 2020 Book of Abstracts. Insights Imaging 11, 34 (2020). pp. 554-555.

Further international publications:

V.I. Óriás, **M. Gyánó,** I. Góg, D. Szöllősi, D.S. Veres, Z. Nagy, C. Csobay-Novák, Z. Oláh, J.P. Kiss, S. Osváth, K. Szigeti, R. Zoltán, P. Sótonyi: Digital Variance Angiography as a Paradigm Shift in Carbon Dioxide Angiography. Invest Radiol. 2019 Jul;54(7):428-436. **IF: 6,091**

Other publications

E. Sipter, **M. Gyánó**, D. Csuka, Z. Prohászka, Á. Szilágyi, P. Pánczél, I. Karádi, N. Hosszúfalusi: The possible role of Epstein-Barr virus in the development of type 1 diabetes mellitus, Diabetologia Hungarica 23 : 1 pp. 39-43., 5 p. (2015)

Book chapter on the subject

E. Dósa, **M. Gyánó**: Lower limb angiography and Sheats in Bartus S., Ruzsa Z. (szerk.): Lower limb interventions. Edizioni Minerva Medica, Turin, Italy, 2018: 24-28 and 36-40 ISBN: 978-88-7711-894-3