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Original Article

Magnetic resonance imaging with dynamic contrast enhancement in perianal fistula staging

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Abstract

Aim: To investigate whether dynamic contrast enhanced perfusion T1-weighted (DCE T1-W) three-dimensional volume interpolated breath-hold examination (3-D vibe) contributes to perianal fistula staging.

Materials and Methods: A total of 110 patients who underwent pelvic magnetic resonance imaging (MRI) (1,5 tesla, Siemens, Avanto) with the preliminary diagnosis of perianal fistula were included in our retrospective study. In our perianal fistula MRI protocol, DCE T1-W 3D vibe sequence was in axial plane with fat-saturation and in five phases (precontrast phase and then in the 45th, 60th, 180th and 240th seconds after intravenous contrast administration). Perianal fistula staging was performed according to T2-weighted sequence findings (acute, subacute, chronic) and by clinical history. Semi-quantitative measurements of the perianal fistula were made with the ROIs placed on the perianal fistula and left femoral artery. Then measurements were made as follows: Type of contrast curve obtained, staining peak time and slope angle of the curve. All measurements were performed independently by two radiologists at different times. Interobserver agreement was also evaluated (Cohen's kappa).

Results: The phases of reaching the peak time (TTP) of contrast increases as the perianal fistula stage increases (mean phases of TTP values were 2.2 th± 1.2 in acute phase fistulas, 2.8 th ± 1.2 in subacute perianal fistulas; 4.4 th ± 1 in chronic fistulas). The angle of inclination decreased as the stage of the perianal fistula increased (42.2 ± 13.2 degrees; 27 ± 11.3 degrees and 9.6 ± 2.3 degrees, respectively).

Conclusion: Diagnosis of perianal fistula with physical examination can be confusing. Sometimes there can be fistulas with different stages in the same patient. Therefore, the use of IV contrast-enhanced pelvic examination with dynamic technique may provide information about the perianal fistula stage.

Keywords: Dynamic contrast enhanced imaging; fibrosis; magnetic resonance imaging; perianal fistula

INTRODUCTION

Perianal fistula is an abnormal connection between the anal canal and the skin. There are the most frequently recurrent perianal abscesses in its etiology. Also includes pathologies such as inflammatory bowel disease, tuberculosis and malignancy. Failure to provide adequate and correct treatment decreases the chances of successful treatment and the recurrence rate increases. The recurrence rate can be up to 25% depending on the failed treatment (1).

Pelvic magnetic resonance (MR) imaging is very important in the diagnosis and typing of perianal fistulas. Correct typing contributes to the surgeon's correct planning. As a result, recurrence can be prevented by correct treatment (1,2).

Pain is the most common complaint in the perianal fistula clinic and discharge is also common. More than one fistula tract or abscess may develop in the same person. Sometimes these fistulas can be in different stages (1,2).

Dynamic contrast enhanced (DCE) MR perfusion imaging technique is used in many systems, especially the oncological field. Studies in the literature have shown that MR perfusion analysis has been helpful in many subjects such as tumor staging and evaluation of response to treatment (3,4). There are studies on the evaluation of fibrosis in liver (5).

Tissue perfusion reflecting neo-angiogenesis can be evaluated in vivo via dynamic contrast T1-weighted MR perfusion methods (3). Quantitative and semi-quantitative measurements that reflect blood flow in the tissues can be made with images taken before and after intravenous (IV) contrast agent administration (3,4).

In our study, patients who underwent pelvic MR with the diagnosis of perianal fistula performed, DCE-MR

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imaging with a total of five-phases. DCE-T1-weighted vibe sequence. We aimed to investigate whether DCE-MR examination contributed to the chronological staging of the perianal fistulas.

MATERIALS and METHODS

Patients

This retrospective study was carried out in a single institution. Study protocol ethics committee approval was received.

A total of 110 patients who had pelvic MR examination with a pre-diagnosis of perianal fistula between January 2016 and December 2017 were included in the study.

Detailed clinical information was obtained from the patients before pelvic MRI. The time to start complaints was clinically questioned. According to the information taken from patients, fistulas were classified as follows: patients whose complaints had been present for 0-2 weeks were classified as group C1 (acute period-active fistula). Those whose complaints continued for 2 weeks to 6 months were classified as group C2 (subacute fistula). Finally, those whose complaints continued for more than 6 months were classified as group C3 (chronic fistula).

Patients who had undergone any surgical intervention for perianal fistula and pediatric age groups were excluded from the study. Patients who had undergone radiotherapy or surgery to the pelvic region for any reason were also excluded. Those with any additional contraindicated condition (those with a pacemaker or stent, claustrophobic patients) for MRI examination were excluded from the study (Figure 1).

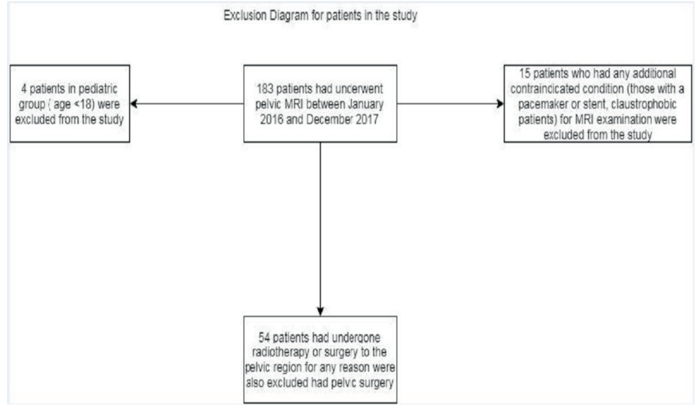

Figure 1. The diagram of the patients excluded from the study for various reasons is followed. A total of 110 patients were included in the study after exclusion from 183 patients who underwent pelvic MRI in our department with a pre-diagnosis of perianal fistula. The diagram summarizes this

MR imaging and analysis

While all patients were in the supine position, pelvic MR examination was performed (1.5 Tesla MR, Siemens Avanto system, Erlangen, Germany) with a phased array abdominal coil. All sequences were taken by holding the breath after a deep inspiration.

The pelvic MR protocol is summarized in Table 1.

Since the anal canal was tilted forward, the reference image was adjusted as a single shot image of the sagittal T2- weighted sequence passing through the center of the anal canal. Other plan images to be obtained were also planned according to the long axis of the anal canal (Figure 2).

Table 1. The table shows the pelvic MR study protocol and sequence parameters that we apply to our patients with perianal fistula

	Perianal Fistula MR Protocol			
Parametres	**T1- weighted TSE**	**DCE 3D T1- weighted vibe**	**Diffusion weighted Imaging (b:0,400,800sec/mm^2)**	**T2- weighted BLADE**
TR/TE (ms)	557/18	4,7/2,3	6250/81	4000/83
FOV (mm)	320	220	220	260
matrix	352x352	256x256	96x96	256x256
ETL				27
FA (0)			10	
Slice thickness/gap (mm)		4/0	4/1	4/1,2
Fat saturation	-	+	-	+
Duration (average)	3min.50sec.	5min. 18 sec.	2min.13sec.	2min. 24sec.

DCE T1-weighted 3D vibe sequence was performed before the administration of gadobutrol at a dose of 0.1 mmol/kg from a peripheral vein at a rate of 2 ml / s and after axial plan 5-phase (45th, 60th, 180th and 240th seconds before and after contrast administrated. T2- weighted BLADE sequences were taken in axial, coronal and sagittal plans with fat suppression technique. (TR: time of repetation TE: time of echp FOV: field of view ETL: echo train length FA: flip angle)

DCE T1- weighted vibe sequence raw data taken in the axial plan was transferred to the workstation with special perfusion software (syngo DynaPBV Body, Siemens). Perfusion color maps were obtained. Semi-quantitative measurements were made with region of interest (ROI) placed on the perianal fistula on these perfusion color maps. In addition, another ROI was placed on the left superficial femoral artery (SFA). Signal-time curves were generated for perianal fistula and SFA. The peak signal reach time (TTP) and the angle measurements of the curve (A) were made on these curves (Figure 3a-c).

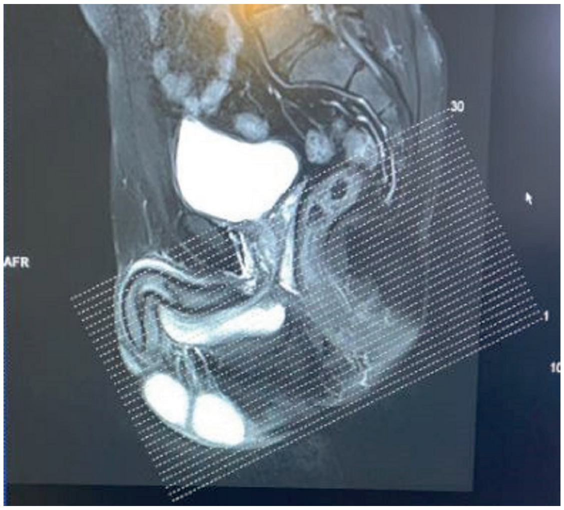

Figure 2. The anal canal was tilted forward and the reference image was adjusted as a single shot image of the sagittal T2-weighted sequence passing through the center of the anal canal. Other plan images to be obtained were also planned according to the long axis of the anal canal

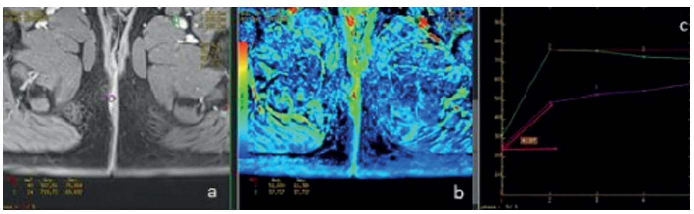

Figure 3. 47 year old male patient; Pelvic MR (1.5 Tesla MR, Avanto, Siemens) was examined in the rectal area with complaints of pain and discharge after intravenous (IV) contrast agent administration (from the left antecubital vein at a dose of 0.1 mmol / kg at a rate of 2 ml / s) DCE (dynamic contrast enhanced) T1-weighted three-dimensional volume interpolated breath-hold examination (3D vibe) sequence image is observed (a). Round pink ROI (examination area) placed on the perianal fistula is observed (a). Color perfusion map obtained from the workstation with special perfusion software programme (b). This image shows the ROI-1 (pink ROI) placed on the perianal fistula and the ROI-2 (green ROI) placed on the left superficial femoral artery (SFA). In both ROI, the surrounding structures are set to be excluded. The final image (c) shows the signal (y-axis) - time (x-axis) curve created as a result of the measurements made from the color perfusion map: the numbers on the x-axis correspond to the phases of our dynamic analysis. In other words, the graph shows the signal change curve between the 1st and 5th phases. The upper green curve shows the left SFA signal change over time, the lower pink curve shows the time dependent signal change of the perianal fistula. SFA's time to reach its peak signal (TTP) is in phase 2. The signal of the perianal fistula rises with a slope similar to the artery curve to 3rd phase, and the angle of inclination (A) is measured at 41 degrees. After the second phase, signal loss begins in our arteries, while the signal increase continues with a slower rise in the perianal fistula

In addition, according to T2-weighted BLADE sequence findings, fistulas were divided into three groups. These groups were as follows: Group B1: the perianal fistula tract is hyperintense, with an air-dependent signal void and / or an intense edema signal in the ischioanal fossa and / or abscess, Group B2: those with perianal fistula tract hyperintense and edema signal in ischioanal fossa, Group B3: those with a perianal fistula tract in the form of a linear hypointense line and no edema signal in the ischioanal fossa.

Independently of each other, two radiologists (10 years and 6 years experienced in abdominal radiology, respectively) who did not know the clinical history of the patients made all measurements. Interobserver correlation was assessed by Cohen's kappa (κ) test.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (version 22.0; SPSS Inc., Chicago, IL, USA).

The distribution of outcome categories was assessed using the Shapiro-Wilk test. Data are presented as mean ± standard deviation, based on the normality of data. And categorical variables were reported as counts and percentages. Statistical significance p-value was accepted as $p < 0.05$.

Consistency between the two observers was evaluated using the Kappa test. Correlation coefficient (κ) values between classes κ <0,4 poor concordance; κ = 0.4-0.6 moderately concordance; κ = 0.6 -0.8 shows a good concordance and κ> 0.8 shows a very good concordance.

RESULTS

According to the clinical history, the distribution of patients into the groups was as follows: 39 patients (35%) in group C1; 56 patients (50%) in group C2 and 15 patients (15%) in group C 3.

According to T2-weighted BLADE sequence findings, there were 42 patients (38%) in group B1, 53 patients (48%) in group B2, and 15 patients (13%) in group B3 (κ = 0.76; p <0.05).

Since there was no statistically significant difference between the classifications made according to clinical classification and according to T2- weighted BLADE sequence, the groups were classified as groups 1, 2 and 3.

When perfusion curves obtained from perfusion color maps created from DCE T1- weighted vibe sequence images evaluated;

The perianal fistula enhancement curve was consistent with the enhancement curve obtained from SFA in Group 1 (average TTP value: 2.2 ± 1.2th phase, A: 42.2 ± 13.2 degrees) (κ=0.82; p<0.05) (Figure 4a-d).

Average TTP value in patients with group 2 perianal fistula: 2.8±1.2th phase, A: 27±11.3 degrees (κ=0.86; p<0.05).

Average TTP value in patients with group 3 perianal fistula: 4.4 ±1.3th phase; A: 9.6±2.3 degrees (κ=0.93; p<0.01).

When the dynamic curve slope obtained from the perianal fistula was similar to the curve obtained from SFA, the findings were consistent with active fistula disease (κ=0.76; p<0.05). (Figure 3a-c).

The contrast dynamics of group 2 were not significantly different as the other two groups (p>0.05). In some group 2 patients, the dynamic curve was observed to have a plateau after reaching the TTP value. In the other part group 2 patients, after reaching the TTP value, an increase was observed in the curve with a slow acceleration (Figure 4a-d). No statistically significant relationship was found when compared with the clinical history of the patients (p> 0.05).

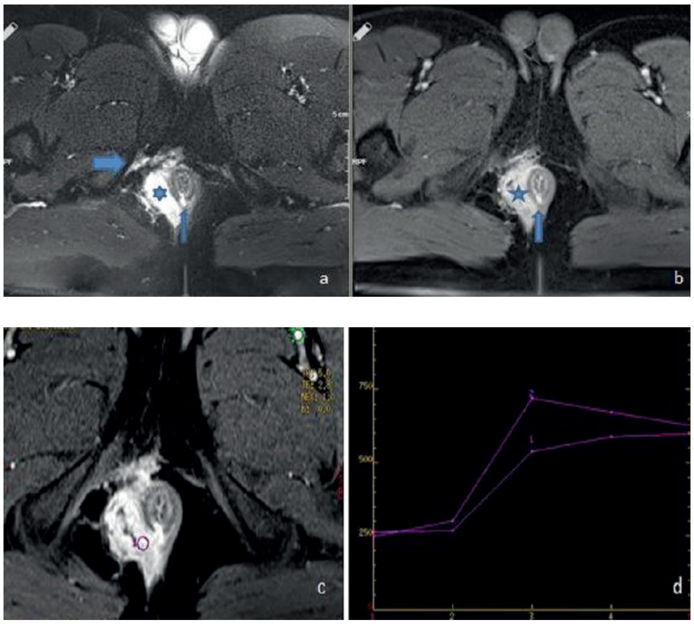

Figure 4. a,b: 39-year-old male patient; T2-weighted image (a) and T1-weighted 3D vibe sequence image after IV contrast agent (b) are observed in the pelvic MRI examination for approximately 10 days with complaints of fullness, pain, and discharge in the rectal area. The perianal region with an inter-sphincteric extension (thin blue arrow) at 6-7 o'clock, and an associated abscess pouch (marked with a blue star) in the extra-sphincteric area is observed. In the perineal fatty tissue, the T2 signal increased significantly in favor of acute inflammation in the anterior (thick blue arrow in figure 2a). This patient was included in group 1 in our study

c,d: Perianal fistula-abscess junction marked with pink ROI (ROI-1) on T1-weighted 3D vibe sequence image of the same patient; the left SFA is marked with a green ROI (ROI-2) (c). The signal-phase time graph curves 1 and 2 obtained from the measurements belong to ROI-1 and ROI-2, respectively. As seen in the signal-phase time curves, the perianal fistula enhancement curve (curve 1) is similar to the left SFA curve (curve 2). The time for both curves to reach the peak signal (TTP) is just before Phase 3. The tilt angles are similar and above 40 degrees. The clinical history and pelvic MR findings (T2- weighted sequence, T1- weighted 3D vibe sequence, and perfusion curve) were found to be compatible with the patient

The patients in Group 3 were compatible with the fistula at the clinical recovery stage and there were signs of fibrosis in the T2- weighted sequence (Figure 5a-c). In the dynamical curves obtained from the fistula of these patients, it was observed that perfusion after the 4th phase increased slowly or showed plateau ($\kappa=0.89$; $p<0.01$) (Figure 5d-e).

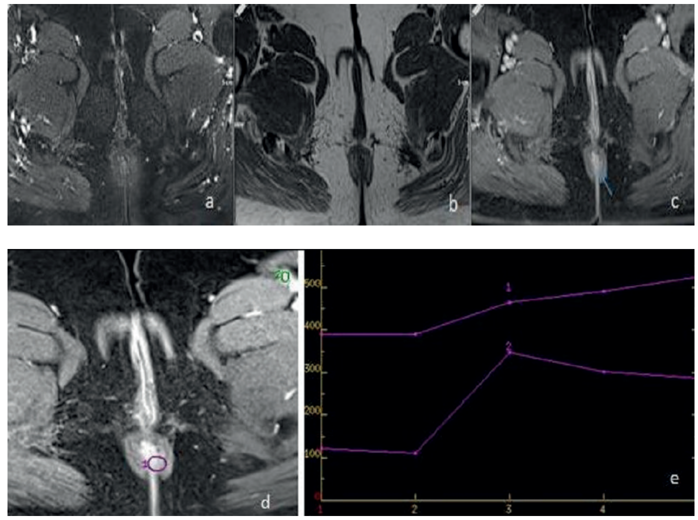

Figure 5. a-c: 56-year-old female patient; The patient who described intermittent pain and occasional discharge for about 5-6 months. However, in the pelvic MR examination sequences, the edema signal is not observed in T2-weighted sequence (a) and in T1-weighted turbo spin echo (TSE) sequences (b) in perianal regions. DCE (dynamic contrast enhanced) T1-weighted three-dimensional volume interpolated breath-hold examination (3D vibe) sequence image is obtained after IV contrast agent administration (left antecubital vein, 0.1 ml / kg dose of gadobutrol at a rate of 2 ml / s) (3D vibe) c). Thin intersphincteric fistula (thin blue arrow) is observed at the perianal region at 5-6 o'clock (c). Due to the absence of concomitant fatty tissue edema, T2- weighted sequence findings were included in group 3 in our patient classification

d, e: On the T1-weighted 3D vibe sequence of the same patient, a simple perianal fistula with an intersphincteric extension at 5-6 o'clock is marked with a green ROI (ROI-2) (d). Signal-phase time curves obtained from ROIs are followed (e). The upper curve (number 1) is the signal-phase time curve of the perianal fistula, and the time to reach the peak signal (TTP) continues with a slow increase until 5th phase. The angle of inclination (A) is below 15 degrees. The bottom curve (number 2) is the signal-phase time curve obtained from SFA, it is noteworthy that the TTP value is just before the 3rd phase and the signal gradually decreases in the advanced phases. It is remarkable that the curves obtained with the T1-weighted 3D vibe sequence contributed to the T2-weighted sequence findings in the case where the chronological staging of the perianal fistula was performed with the findings identified

DISCUSSION

In the field of oncology, especially in abdominal radiology and neuroradiology, DCE T1-weighted MR imaging has proven to be a clinically useful, non-invasive functional imaging technique to measure tumor vascularity and tumor perfusion properties (3,4).

DCE T1-weighted MR imaging can show blood flow, hypoperfusion areas in the tissue of interest, thereby assisting treatment selection(4). It also has the potential to provide information about endothelial permeability and micro-vessel density variations to ensure frequent monitoring during treatment and to evaluate response to treatment (4,6).

In patients who underwent liver biopsy and retrospectively evaluated by DCE T1-weighted sequence with 4-phase, a significant positive correlation was found in later stages of hepatic fibrosis, especially with the signal measured in the latest phase of DCE T1-weighted sequence (7).

In our study, we aimed to investigate whether DCE T1-weighted vibe sequence with five-phase contributed to the perianal fistula chronological staging. We compared our findings with the T2- weighted BLADE sequence findings and clinical history taken from the patients.

It was noteworthy that perianal fistula perfusion started between 60-180 seconds in all groups, similar to the other studies in the literature (6,8).

Perianal fistula is seen as a linear tract in MRI and other imaging modalities. Signal changes suggesting active inflammation are also seen in the surrounding tissue. The presence of air in the fistula tract is significant in terms of active disease (6-9). In our study, we showed that the fistula tract enhancement pattern can also provide information about disease activation.

The group with a curve similar to the dynamic curve obtained from SFA could be interpreted in accordance with the acute period, active fistula, which is a relative assessment. Since the curves obtained are affected by the hemodynamics of the patient, it is more appropriate to evaluate this way. The angle of the curve obtained from fistulas in the chronic period was generally below 11 degrees. This can be interpreted due to slow and late enhancement due to the fibrotic process (6,7).

However, our study has some limitations. As indicated in the literature, Dynamic MR perfusion sequences are required to be taken at 15-second intervals to determine the early staining and capillary transition time of the pathology (8,10). As a result, in addition to semi-quantitative measurements of signal intensity changes over time, it is possible to use a quantitative approach based on the pharmacokinetic model of the contrast agent (8,11). We could not show this in our study. We were able to make semi-quantitative and visual evaluation.

However, obtaining the sequence after IV contrast administration with 3D vibe technique allowed us to obtain a multiplanar reformat image. In addition, it was possible to obtain conventional fistulography-like images with high contrast resolution as a result of subtraction technique via post-processing. The absence of radiation exposure is also an important advantage, especially for the younger age group.

Another limitation of our study is that we could not confirm perianal fistula staging with histopathology.

However, considering that there is the possibility of having more than one fistula in a patient, the DCE 3D T1-weighted vibe sequence has made significant contributions in determining which perianal fistula is active or in the recovery phase.

T2-weighted sequences are of great importance in pelvic and abdominal MRI. However, because of their long acquisition time, they are susceptible to motion artifacts. With the subtraction technique and other saturation techniques that can be added, it is possible to increase the image quality of the DCE T1-weighted sequence (8-11).

Consequently, in the diagnosis of perianal fistula and about guiding treatment and follow-up, pelvic MR with 3D T1-weighted vibe sequence provides more accurate perianal fistula staging. And especially in patients with clinical examination difficulties (children and elderly groups with communication difficulties) can contribute to the diagnosis of fistula.

CONCLUSION

In the study conducted by Sahnan et al., 3D perianal fistula models obtained from T2- weighted BLADE sequence images obtained in three plans could be created in detail (12). The probability of obtaining a continuous image with the BLADE sequence is more difficult compared to the T1-weighted vibe sequence.This can cause data loss. In T2- weighted BLADE sequence, the image sharpness increases in the FOV field. The contrast in the image is determined by the T2 signal of the surrounding organs and structures. This may require some preparation in terms of image contrast optimization (such as an antiperistaltic agent before MRI, bladder full) (13,14).

However, 3D images with higher temporal resolution can be obtained with the T1- weighted vibe sequence to be added to the T2- weighted BLADE sequence. This may be the subject of a future study.

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REFERENCES

1. Criado JDM, García L, Fraga P, et al. MR Imaging Evaluation of Perianal Fistulas : Spectrum of Imaging. RadioGraphics 2012;32:175-94
2. Daabis N, Shafey R El. Magnetic resonance imaging evaluation of perianal fistula. Egypt J Radiol Nucl Med 2013;44:705-11.
3. Gaa T, Neumann W, Sudarski S, et al. Comparison of perfusion models for quantitative T1 weighted DCE-MRI of rectal cancer. Scientific Reports 2017;7:12036
4. Hameeduddin A, Sahdev A. Diffusion-weighted imaging and dynamic contrast-enhanced MRI in assessing response and recurrent disease in gynaecological malignancies. Hameeduddin and Sahdev Cancer Imaging 2015;15:3
5. Gilbert ÃG, Nguyen ÃBN, Tang A. Liver Fibrosis Quantification by Magnetic Resonance Imaging. Top Magn Reson Imaging 2017;26:229-41.

6. Heye T, Davenport MS, Horvath JJ, et al. Reproducibility of Dynamic Part I . Perfusion Characteristics in the Female Pelvis by Using Multiple Computer-aided Diagnosis Perfusion Analysis Solutions. Radiology 2013;266:801-11.
7. Keller S, Aigner A, Zenouzi R, et al. Association of gadolinium-enhanced magnetic resonance imaging with hepatic fibrosis and inflammation in primary sclerosing cholangitis. PLoS ONE 2018;13: e0193929
8. Tofts PS. T1 -weighted DCE Imaging Concepts: Modelling, Acquisition and Analysis. Magnetom Flash 2010;1-5
9. Ippolito D, Lombardi S, Franzesi CT, et al. Dynamic Contrast-Enhanced MR with Quantitative Perfusion Analysis of Small Bowel in Vascular Assessment between Inflammatory and Fibrotic Lesions in Crohn' s Disease : A Feasibility Study. Hindawi Contrast Media & Molecular Imaging Volume 2019, Article ID 1767620
10. Mazaheri Y, Akin O, Hricak H. Dynamic contrast-enhanced magnetic resonance imaging of prostate cancer: A review of current methods and applications. World J Radiol 2017;9:416-25.
11. Gordon Y, Partovi S, Müller-eschner M, et al. Dynamic contrast-enhanced magnetic resonance imaging : fundamentals and application to the evaluation of the peripheral perfusion. Cardiovasc Diagn Ther 2014;4:147-64.
12. Sahnan K, Adegbola SO, Tozer PJ, et al. Innovation in the imaging perianal fistula: a step towards personalised medicine. Therap Adv Gastroenterol. 2018; 11:1756284818775060
13. Zand KR,Reinhold C,Haider MA, Nakai A, et al; Artifacts and Pitfalls in MR Imaging of the Pelvis;J. Magn. Reson. Imaging 2007;26:480-97.
14. Krupa K,Bekiesińska-Figatowska M; Artifacts in Magnetic Resonance Imaging;Pol J Radiol 2015;80: 93-106.