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Article

Diagnosis of perianal fistula with diffusion-weighted MRI

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Abstract: Background: Contrast enhanced T1- weighted (CE-T1W) magnetic resonance imaging (MRI) is the preferred imaging modality for assessing perianal fistulae (PAF), it provides accurate detection and characterization of PAF. The study aims to assess the use of diffusion weighted MRI (DWMRI) alone as an alternative approach to CE-T1W-MRI and the identify optimal *b*-values in the obtained DWMRI for assessing anatomy and pathophysiology of PAF. **Methods:** 37 perianal fistula (PAF) patients who are in preoperative procedures with an average age of 40 ± 11.5 years, were recruited in this study. All patients were imaged on a 3.0 Tesla MRI scanner using CE-T1W sequence and DWMRI for *b* values of 50, 400, 800 and 1600 s/mm^2. The ratio of the mean region of interest (ROI) that is measured from 50% of the maximum for the lesion to a reference background in images of both approaches. Coefficient of variation was also applied in the assessment of the two approaches. The analyses were carried out using the Mann-Whitney U test. **Results:** ROI measurements were 203 ± 48 and 68 ± 24 in the ROI of the lesion, and 116 ± 20 and 31 ± 6 for the reference background ROI for CE-T1WMRI and DWMRI, respectively; the values were represented as mean ± STD. The lower *b* value (<100 s/mm^2) of DWI reveals higher image resolution of the anatomical structures compared to higher *b* values; however, higher *b* values were better than lower *b* values in image contrast. The percentage of coefficient of variation was not statistically significantly different between CE-T1WMRI and DWMRI (*p*-value = 0.079). **Conclusions:** The findings show that DWMRI has statistically similar efficacy with respect to CE-T1WMRI in the diagnosis of PAF. Thus, this may suggest that DWMRI ought to be regularly included in typical MRI procedures for diagnosing PAF.

Keywords: perianal fistula; DWMRI; T1W; MRI; intersphincteric; trans-sphincteric

1. Introduction

Perianal fistula (PAF) is a chronic abnormal passageway between two epithelial surfaces that is called a fistula. Such fistulas can form between intestinal loops (enteroenteric), the intestine and the skin (enterocutaneous), or the rectum and the skin around the anus (perianal) [1]. This condition (PAF) can be quite uncomfortable, and it is often seen in people who have inflammatory bowel disease. Middle-aged men are twice as likely to develop these fistulas as women [2].

Consequently, PAF is a growing health concern, leading to substantial morbidity, impaired quality of life, and causing anxiety to the patient [3]. Moreover, it is an underlying cause of anal gland inflammation or secondary malignancy [4,5], and can also be a breeding ground for the systemic spread of infection [6]. Records have shown that a PAF, in addition to its incidence rate, which is doubled in middle-aged men compared to women [2], the recurrence rate is considered very high and reaches up to 50% of all PAF cases [7].

The PAFs are believed to affect nearly about 20% of CD patients [8]. The treatment of PAF typically involves surgery to remove all sources of infection in the fistula and its tract, while protecting the anal sphincter function. However, managing PAF faces many challenges, which may lead to an increased likelihood of treatment failure and recurrence rates, leading to substantial morbidity and repeated surgeries [9]. Therefore, to achieve positive surgical results, a complete preoperative assessment of fistula characteristics and associated findings is essential. Thus, this necessitates the development of improved imaging techniques to guide surgical interventions.

Fistulography and Ultrasonography as a preoperative evaluation means throughout the imaging for PAF were utilized. Yet, they could not provide all the required information for assessing PAF due to their limited spatial resolution and the sensitivity of assessing PAF [9,10]; thus, they are of less benefit for surgical management. Although the latter was shown to be a good option due to its availability and rapidity, in addition to the safety concerns [10].

Computed tomography (CT) is an imaging modality that could also be used in assessing PAF. The CT scan takes great advantage of the rapid acquisition of images and three-dimensional visualization, in addition to the advanced algorithms employed in modern CT scanners that enhance the clarity and contrast of the images, allowing for better visualization of pathologies. As a result, CT scan not only streamlines the diagnostic process but also significantly contributes to improved patient outcomes by guiding appropriate treatment decisions quickly and efficiently. Nonetheless, the use of ionizing radiation, especially in the case of younger individuals and during pregnancy, is a major concern for the use of CT scan in the diagnostic setting of PAF [11]. Besides, CT scans are not detailed enough to analyze fistula anatomy due to the fact that sphincter and pelvic floor muscles have similar attenuation values in CT images as fistula [10]. Additionally, CT scan finding in the assessment of PAF was also found to be comparable to physical examination [12].

Magnetic resonance imaging (MRI), due to its three dimensional appraisal and excellent soft tissue resolution, confers a distinct advantage in accurate detection and characterization and allows for absolute quantification for assessing anatomy and pathophysiology of PAF. Thus, it is considered a standard imaging modality in this situation, and it is more consistent with surgical findings than any other imaging modalities [13-17]. It is also better than the CT scan for PAF due to its higher contrast resolution [18].

For characterizing PAF anatomy and pathophysiology (its extensions, secondary tracts, horseshoe configurations, and abscesses), contrast enhanced T1 weighted (CE T1W) MRI and fat suppression are superior to other MRI sequences [19]. Hence, they give enough information to guide PAF surgical intervention and distinguish a fluid-filled channel from a region of inflammation [20].

However, the administration of the gadolinium contrast agent is accompanied with several risks and limitations. These are the limited use of gadolinium contrast agent in renal dysfunction patients, prolonged MRI scanning, and added expense [21,22]. In addition to long-term safety for the administration of contrast agents, such as the possibility of accumulation of gadolinium chelate in the brain, bone, and skin [23].

Alternatively, the utilization of the diffusion weighted MRI (DWMRI) technique provides a novel approach to improve the capabilities of MRI, without the need for contrast agent administration [24]. Findings indicate that DWMRI improves the ability to discriminate between lesions (inflammatory bowel disease, cancer) and surrounding tissues [24,25]. The DWMRI was also found to be appropriate in evaluating the activity of PAF and spotting patients who are at an increased risk of recurrence [26].

Where the changes in water mobility (Brownian motion) caused by cell membranes and tissue are shown in DWMRI [27]. Water molecule diffusion in tissue decreases as cellularity and cell membrane integrity increase. The higher cellular density of inflammatory tissues restricts water diffusion, differentiating them from healthy tissue in DWMRI by qualitative assessment using relative signal intensity and quantitative assessment in calculating apparent diffusion coefficient in DWMRI [25,28]. Subsequently, the obtained DWMRI varies in the image contrast as a function of the used b values in DWMRI settings [29]. Thus, differences in DWMRI protocols, including b-values, among various studies can affect the comparability of findings. Therefore, standardization of these protocols is essential to guarantee reliable and consistent evaluations. Therefore, selecting the best b values in DWMRI for evaluating the anatomy and condition of PAF is critical.

The current study aims to assess the utilization of DWMRI alone or combined with other MRI sequences and for several b values in detecting the perianal fistula for patients with suspected PAF and in the preoperative procedure, as an alternative method to post contrast enhanced (CE) MRI for patients who are not candidates for receiving gadolinium contrast.

2. Materials and methods

A total of thirty seven patients who were thought to have a PAF disease were included in this study with the approval of the institutional review committee. These enrolled patients were sent to the MRI unit for scanning for the suspicion of PAF disease. The recruitement of participants was under the following exclusion criteria; patients who had surgery in the past (as per patient's history), patients who had recurrent perianal disease and patients who could not receive gadolinium contrast due to their medical condition that made it unsafe for them to use gadolinium or had claustrophobia of getting an MRI scan, those kind of patients were not part of this presented study.

A 3.0 Tesla MRI scanner with 18 channels of body phased array coils (MAGNETOM Skyra, Siemens, Erlangen, Germany) was used to scan every subject who participated in this study.

The imaging techniques "sequences" that were included are CE T1W sequence, T1 weighted MRI (T1W MRI), fat suppressed T1W MRI, and Short Tau Inversion Recovery (STIR). All of these imaging techniques were performed in the axial plane.

DWMRI was added with the following criteria: axial orientation, the TE (echo time) and TR (repetition time) were set to 70 milliseconds (ms) and 4500 ms, respectively; the slice thickness was 3 mm with a gap of 0. 6 mm between slices; the total of 30 slices were taken during the imaging process; the data were reconstructed into an image array of 128 × 128 of active pixels; the field of view (FOV) was set to 350 mm; the number of excitations (NEX) value was set to 1; the b values used in the

DWMRI imaging were 50, 400, 800, and 1600 s per square millimeter (s/mm^2).

For the T1W sequence, the acquisition parameters were as follows: axial, TE/TR = 11/350 ms; slice thickness = 3.5 mm; interslice gap = 0.7 mm; matrix size = 128 × 128; and FOV = 350 mm.

Gadolinium containing contrast agent (Dotarem Gadoterate Meglumine of 0.5 millimoles per millilitre (mmol/mL) was administered intravenously at a concentration of 0.2 mL for every kilogram of body weight (0.2 mL/kg) and at a rate of 2 mL every second (2 mL/s). The total scan time was approximately 25 min.

The statistical analyses were carried out using MATrix LABoratory (MATLAB) software, version R2016b. Comparing the CE T1W MRI and DWMRI was assessed with the percentage of coefficient of variation (%CV), which is defined as the percentage standard deviation (STD) between the mean of every ROI measurement relative to the ROI mean [30]. The mean of the ROI signal was measured from 50% of the signal peak (maximum). This approach is to focus on the most significant data points without being influenced too much by extreme values that might skew the results. The analyses were carried out using Mann Whitney U test. The *P* value of less than 5% was deemed statistically significant.

3. Results

The average age of the 37 patients enrolled in this study was 40 ± 11.5 years. Of the patients, 23 had intersphincteric fistulas (62%), and 14 had trans sphincteric fistulas (38%). There were 32 men (86%) and 5 women (14%) of the patients who were recruited. In 16 patients (43%), an abscess was noted.

Figure 1 displays the distribution of the calculated mean signals of ROIs for both CE T1W MRI and DWMRI images. The CE T1W MRI data is represented by star markers, with a dotted line indicating the fitted regression line. The DWMRI data is represented by x markers, with a solid line indicating its fitted regression line.

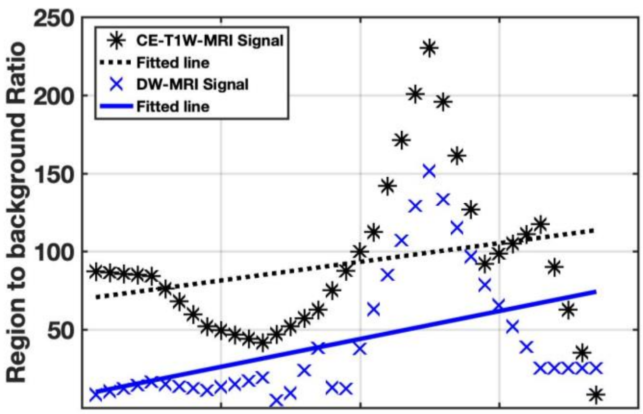

Figure 1. Distribution of mean signals of ROIs to the background ROI signal for 37 patients with the fitted lines (dotted line is the fitted line for CE T1W MRI, and solid line is the fitted line for DWMRI).

Table 1 below presents the mean, maximum, and minimum values with STD of the calculated signals of ROIs for MRI images of all recruited participants (37 patients). It provides a concise overview of the range and central tendency of the ROIs under consideration.

Table 1. The data of signal value of ROI (mean, maximum, minimum and standard deviation "STD") for 37 patients.

		Mean ± STD	Maximum	Minimum
CE T1W MRI	ROI of Lesion	203 ± 48	318	95.0
	Background ROI	116 ± 20	160	69.0
DWMRI	ROI of Lesion	68.0 ± 24	122	21.0
	Background ROI	31.0 ± 6.0	45.0	17.0

In **Figure 2**, the diagnosis of inter sphincteric PAF is conducted by utilizing both CE T1W MRI and DWMRI, with the latter specifically applied at a b value of 100 s/mm^2. This dual imaging approach enhances the diagnostic accuracy by leveraging the strengths of both techniques (CE T1W MRI and DWMRI); CE T1W MRI provides superior anatomical details and vascular enhancement, while DWMRI offers insights into the cellular density and microstructural integrity of the affected tissues. The evaluation revealed a remarkable signal to background ratio, with CE T1W MRI reaching a maximum signal ratio of 86% and for DWMRI the signal to background ratio is reaching 70%.

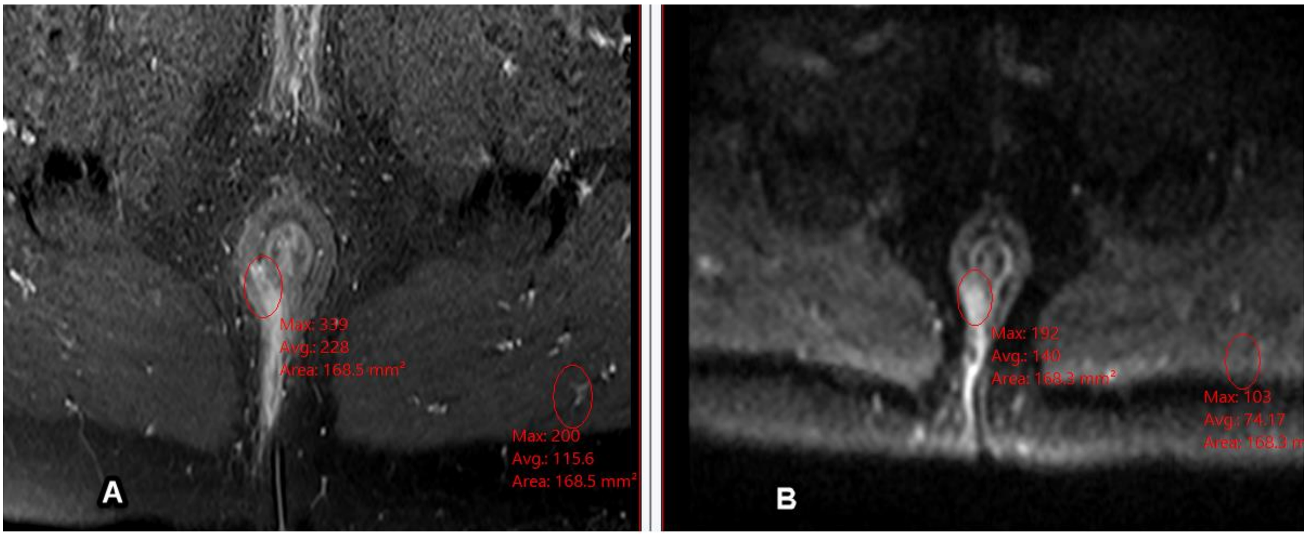

Figure 2. A 41 years old male with inter sphincteric perianal fistula. **(A)** Axial CE T1W MRI image shows high signal intensity fistula (ROI); **(B)** axial DWMRI image shows high signal intensity for the same ROI.

In **Figure 3**, the diagnosis of inter sphincteric PAF is achieved through a comprehensive analysis utilizing both CE T1W MRI and DWMRI. Notably, the DWMRI image was conducted with a *b* value of 100 s/mm^2, in a 52 year old male patient; this setting helps to provide a clear image of the inter sphincteric.

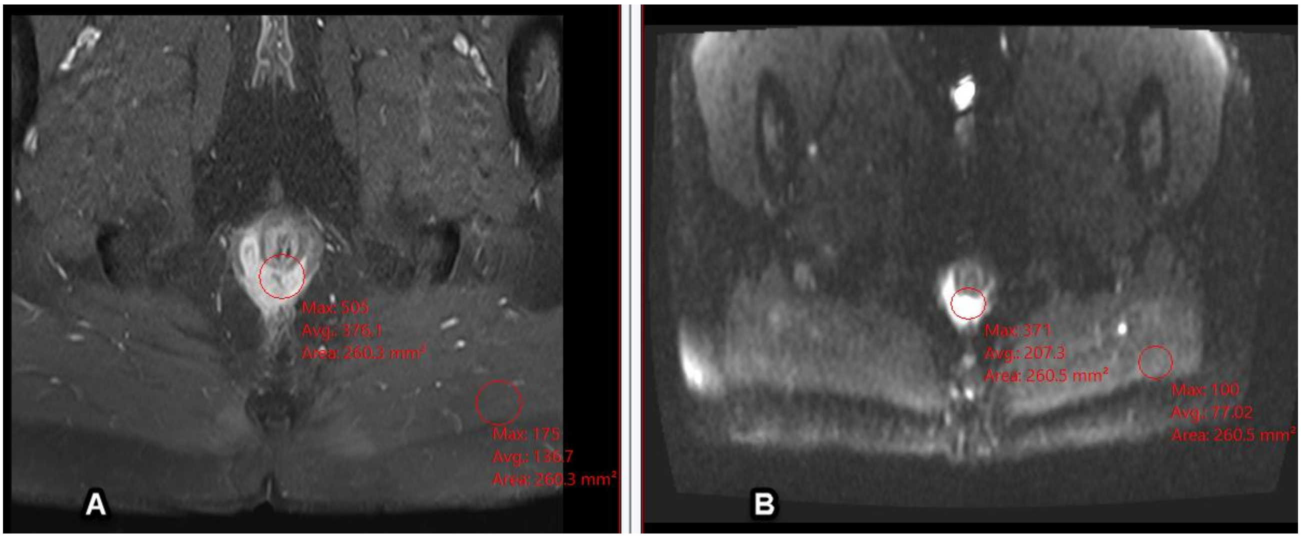

Figure 3. A 52 years old man with inter sphincteric perianal fistula. **(A)** Axial CE T1W MRI image shows high signal intensity fistula (ROI); **(B)** DWMRI image for *b* value of 100 s/mm^2, and it shows high signal intensity for the same fistula (ROI).

CE T1W MRI for a 38 years old female with inter sphincteric PAF is shown in **Figure 4A**. In addition to CE T1W MRI (**Figure 4A**), DWMRI image was employed to further delineate the characteristics of the affected area, utilizing different *b* values to enhance the contrast. Specifically, **Figure 4B** illustrates the DWMRI results obtained at a *b* value of 100 s/mm^2, which is particularly useful for assessing the cellularity of the lesion and identifying any inflammatory processes. Meanwhile, **Figure 4C** presents the finding at a higher b value of 300 s/mm^2, offering a more sensitive evaluation of restricted diffusion, which can be indicative of abscess formation.

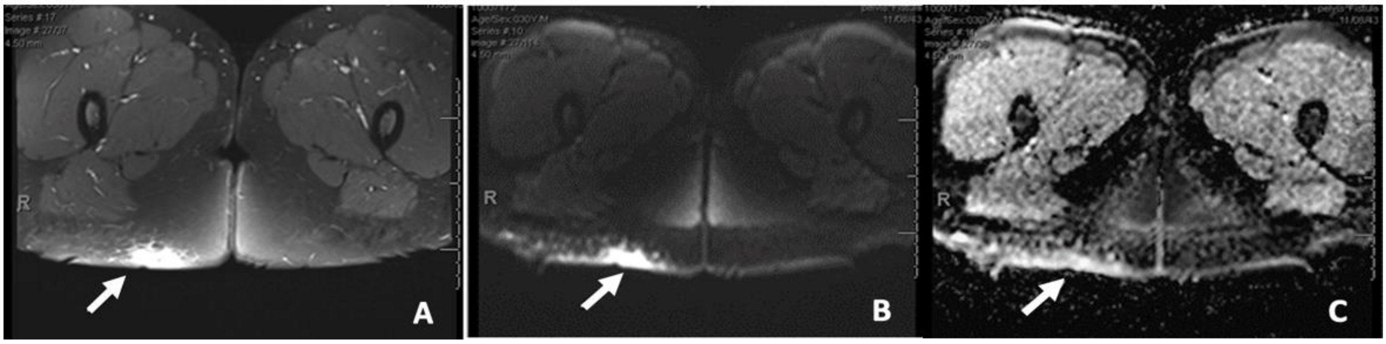

Figure 4. A 38 years old female with inter sphincteric perianal fistula, images are shown a right gluteal small superficial abscess formation. **(A)** Axial CE T1W MRI image; **(B)** DWMRI with a *b* value of 100 s/mm^2 and **(C)** a *b* value of 300 s/mm^2.

Figure 5A displays the axial CE T1W MRI of a 41 years old male patient with fistula in ano and edema, which provides a detailed view of the anatomical structures surrounding the affected area, highlighting the extent of the edema. **Figure 5B,C** complement this analysis by presenting DWMRI images with varying *b* values (100 s/mm^2 in **Figure 5B** and 300 s/mm^2 in **Figure 5C**). The lower *b* value (100 s/mm^2) in **Figure 5B** may reveal higher image resolution of the anatomical structures. However, a higher *b* value resulted in better contrast than a lower *b* value DWMRI (**Figure 5C**).

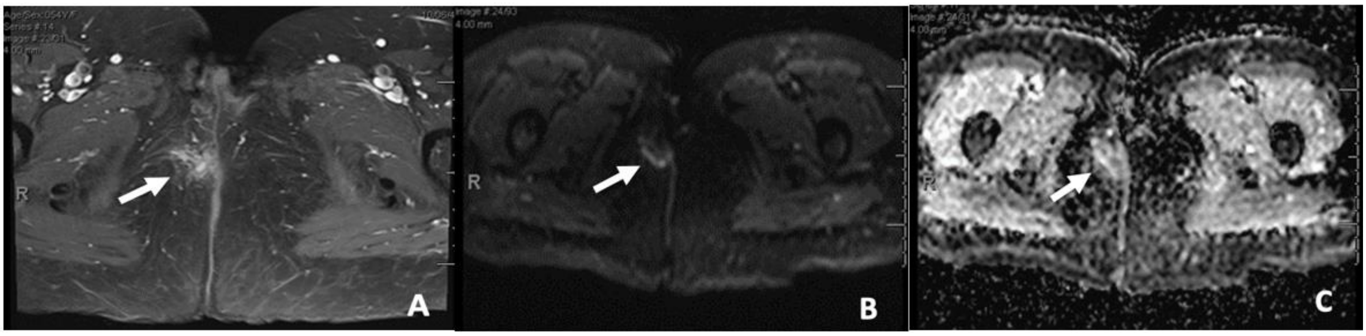

Figure 5. A 41 years old male, images show fistula in ano with edema. **(A)** Axial CE T1W MRI image; **(B)** DWMRI with *b* value of 100 s/mm^2 and **(C)** *b* value of 300 s/mm^2.

When we looked at how well we could find fistula activity, we discovered that the results for two techniques of MRI scan (CE T1W MRI and DWMRI) were quite similar. This means that both types of techniques showed about the same level of ability to detect the activity of fistulas. Both CE T1W MRI and DWMRI did not vary statistically; the p value, as determined by the Mann Whitney U test, was 0.079 (p value > 0.05). A box and whisker plot is used to demonstrate this statistical analysis (it is illustrated in **Figure 6**).

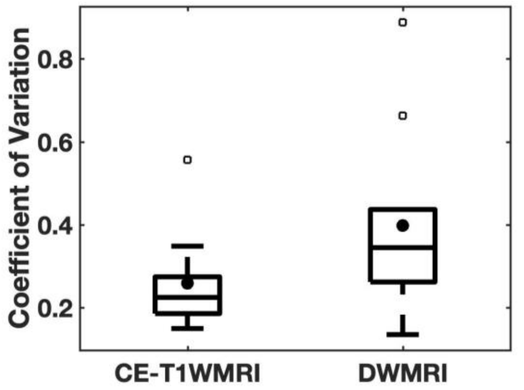

Figure 6. Box and whisker plot illustrates a compelling comparison of cv% for both CE T1W MRI and DWMRI; the *p* value associated with this comparison is 0.079.

4. Discussion

The PAF, a fairly common condition, is an abnormal channel near the anus. To successfully operate on PAF, surgeons must locate the main and secondary channels and determine their position relative to the sphincter muscles for effective fistula repair and abscess removal (if needed). A physical exam alone might be insufficient to identify these features; recurrence often stems from undetected infection sources during the initial operation [31]. Therefore, advancing medical imaging techniques for surgical guidance to improve surgical precision and efficiency is essential. The most imaging modalities used for PAF diagnosis are Ultrasound and MRI.

Ultrasound is a radiation-free, cost-effective, widely available imaging modality and a fairly precise imaging technique for assessing PAF [32]. Moreover, the introduction of three-dimensional endoanal ultrasound has further enhanced the ability to diagnose PAF and improved the accuracy in viewing the PAF track and identifying interior openings [33]. However, the operator dependency and restricted tolerance of patients (three-dimensional endoanal), as well as the limited capability in delineating the fibrotic pathways due to bowel gas and limited contrast of soft tissue, are important drawbacks of the ultrasound imaging modality [34–36].

MRI is a non-invasive imaging modality, lacks of ionizing radiations, identifies fistulous tracts and associated abscess, state of fistula healing, whether a fistula is active or a chronic scar, postoperative features, differentiation of perianal fistulas from other conditions and also provides excellent anatomical detail, thus helping surgeons to plan surgery accordingly and reducing the risk of complications like fecal incontinence [37,38].

The PAF and its complications are now being diagnosed using CE T1W MRI. The CE T1W MRI is much more consistent with surgical findings than any other imaging modalities used for this condition [39]. Thus, CE T1W MRI for assessing PAF is now the de facto standard. The CE T1W MRI is very helpful as it provides clearer and more reliable images compared to other types of imaging used to look at this condition. The major concern of CE T1W MRI is the use of contrast media, which may not apply to all patients.

Using DWMRI would allow for a precise differentiation between the inflammatory process and the surrounding normal tissues, thereby enhancing the diagnostic accuracy [4]. Besides early disease detection, DWMRI offers improved interpretation of postoperative MRI following fistula surgery [40]. The fistulous tract can also be better demonstrated on DWMRI due to the low signal from the surrounding tissue [41]. DWMRI has also been shown to be superior to fat-suppressed T2 weighted MRI images in detecting fistula tracts [40].

Therefore, DWMRI offers a cost-effective alternative to contrast studies, avoiding both the contraindications and extra cost [42]. However, precisely which b values enhance the accuracy of DWMRI parametric maps in PAF settings remains elusive.

Utilizing low *b*-values (ranging from 0 s/mm^2 to 200 s/mm^2) facilitates the identification of the role of tissue micro-perfusion in water diffusion. Although the idea originated in the 1980s, technical limitations hindered its implementation until recent technological progress. The advancement of MRI systems has now enabled the acquisition of low *b*-values [43].

Thirty two of the recruited patients in this current study with PAF were males, and they account 86% of the total recruited patients. In this context, PAF was shown to be more prevalent in males than females throughout tremendous studies [44–48].

Recently, a study by Boruah et al., has reported an accuracy of 79.6% in detecting PAF using DWMRI alone and 98.3% for combined DW T2W MRI. This study was with an average of 3 *b* values (50 s/mm^2, 400 s/mm^2 and 800 s/mm^2) [49]. Another study by Mohsen et al., however, concluded that the visibility of PAF was not significant in comparison between T2W MRI and combined DWMRI with T2W MRI [50]. A study of Dohan et al., demonstrated a high specificity of DWMRI in detecting PAF, with results indicating an impressive specificity rate of 100%. This remarkable level of specificity signifies that DWMRI is exceptionally accurate in identifying patients with PAF, minimizing the chances of false positives. In contrast, the sensitivity of T2W MRI was reported in the same study to be only 91.2%. Additionally, the visibility of fistulas is enhanced with DWMRI imaging compared to T2W MRI [51]. The findings underscore the clinical significance of utilizing DWMRI as a diagnostic tool, suggesting that it could play a pivotal role in clinical settings, particularly in the management and treatment of patients at risk of PAF, ultimately leading to improved patient outcomes and more informed therapeutic decisions.

With respect to a ratio of ROI signal measurement on the lesion from 50% of the maximum to the ROI of a background region for CE T1W MRI images, and with the same settings meticulously applied to DWMRI images for all 37 recruited patients, it is noteworthy that the observed pattern was remarkably similar, as is clearly illustrated in **Figure 1**. This consistency suggests a potential correlation between the lesion characteristics observed in CE T1W MRI images and the diffusion parameters derived from DWMRI.

Figures 2 and **3** illustrate the inter sphincteric perianal fistula in two male patients aged 41 and 52 years, respectively, utilizing axial CE T1W MRI image and axial DWMRI image, labelled as “A” and “B”, respectively. Both imaging techniques (CE T1W MRI and DWMRI) provide an acceptable visualization of the lesion, facilitating a detailed assessment of its characteristics and extent. Remarkably, both CE T1W MRI and DWMRI exhibit comparable spatial resolution and anatomical delineation, ensuring that the surgeon can rely on either technique, as per patient condition, to obtain critical information necessary for diagnosis and subsequent management of the PAF.

In areas with high cellular density, such as in the areas of abscess formation, DWMRI for low *b* value (that is 100 s/mm^2) shows a hypersignal that is shown to be comparable to the CE T1W MRI signal. However, for large *b* values (> 100 s/mm^2), the resolution has deteriorated (**Figures 4** and **5**). Thus, fistula to surrounding structures was easily visualized with a high signal of fistula to background ratio for low *b* values (*b* value ≤ 100 s/mm^2), which allows tissue discrimination as it is also suggested by the study of Takahara et al. [52]. However, DWMRI had a limited spatial resolution. We found a comparable finding between CE T1W MRI and DWMRI in detecting fistula activity, which was quantitatively represented by CV%, indicating the variability in the measurements taken. The statistical analysis yielded a *p* value greater than 0.05, suggesting that there was no statistically significant difference between the two imaging techniques in this specific context of evaluation (**Figure 6**). This revealed that both CE T1W MRI and DWMRI exhibit similar efficacy in identifying the presence and extent of fistula activity, thus providing surgeon with two viable options for diagnostic assessment.

Although combined DWMRI and CE T1WI MRI could improve fistula conspicuity, DWMRI alone may serve as another option for fistula conspicuity when contrast material is contraindicated. Due to the swift scan time (around 3 min) for DWMRI and the wide availability of this sequence in most MRI scanners, in addition to the feasibility of DWMRI to assess the fistula activity. DWMRI may be utilized for assessing PAF and particularly for patients with contraindication to contrast agents. In this context, we recommend the use of b values of 0 and 100 s/ mm^2 as two *b* values in DWMRI for evaluating and assessing the activity PAF. Yet, due to the limited spatial resolution of DWMRI, another sequence with higher spatial resolution may be required for better anatomic orientation, such as fat suppressed T2W MRI as stated in the suggestion of Hori et al. [53]. Therefore, despite the benefits provided by the utilization of contrast enhanced MRI for diagnosing PAF, DWMRI alone or in combination with T2W MRI may provide similar utility, as it has been demonstrated in this current study, and also in the study of Cattapan et al. [54].

There are some limitations in this current study that need to be addressed. First, the number of patients is statistically small (37 participants). The second point to consider is that the data are collected from a single center. Third, the absence of surgical correlation for every case is another limitation, which may affect the validation of the imaging findings, in addition to the consideration of the correlation between surgical and imaging findings. Finally, our assessment did not consider the impact of various treatments on the progression and evolution of the PAF disease. Addressing these limitations has the potential to strengthen the findings, make them more reliable, and improve reproducibility and generalizability.

5. Conclusions

DWMRI has statistically similar efficacy with respect to CE T1W MRI in the diagnosis of perianal fistula. Therefore, DWMRI may be utilized as an alternative approach for patients in whom the contrast agent is contraindicated. Due to the limited spatial resolution of DWMRI, T2W MRI in combination with DWMRI allows better anatomic orientation. In the area of abscess formation, low *b* value ≤ 100 s/mm^2 shows a hypersignal that is comparable to the CE T1W MRI signal. This indicates DWMRI ought to be regularly included in typical MRI procedures for diagnosing perianal fistulas.

Author contributions: Conception and design of the study, MSA and AAM; data analysis and interpretation, MSA; drafting and review of the manuscript, MSA and AAM; compiled the data, AAM; interpreted the results, MSA and AAM; performed ROI measurements, AAM; reviewed the data analysis and offered critical feedback on the manuscript, MYA. All authors have read and agreed to the published version of the manuscript.

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Availability of data and materials: The authors declare that all data supporting the findings of this study are available within the paper.

Institutional review board statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the ethical review board from Ha’il University (Ethical approval No. H-2022-132 on 28/03/2022 G).

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

Conflict of interest: The authors declare no conflict of interest.

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