IN VIVO 40: 364-371 (2026)
doi: 10.21873/invivo.14200

Investigation of the Relationship Between Adrenal Gland Signal Intensity and Age in Whole-body MRI/DWIBS

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Abstract

Background/Aim: To identify factors influencing adrenal signal intensity in whole-body magnetic resonance imaging/diffusion-weighted whole-body imaging with background body signal suppression (MRI/DWIBS).
Patients and Methods: This retrospective study included patients who underwent whole-body MRI/DWIBS at our institution between April 2019 and April 2025 with no malignant tumor or history of a malignant tumor. Adrenal signal intensity and gland area were measured and analyzed according to sex and age.
Results: The study included 22 male patients (average age of 58.2±11.7) and 38 female patients (average age of 55.9±15.4). The maximum signal intensity (max value) of the left adrenal gland on diffusion-weighted imaging was 1,885.5±352.0, and the mean gland area was 1,198±435.0 mm^2 in male patients, and 1,517.1±429.5 and 760.5±325.6 mm^2, respectively, in female patients. The median values for max value of the left adrenal gland on diffusion-weighted imaging were significantly larger in male patients (male: 1855 *vs.* female: 1,472, p<0.01). The median value for adrenal gland area was significantly larger in male patients (male: 1,159 mm^2 *vs.* female: 768.5 mm^2, p<0.01). Among female patients, those aged <40 years had a significantly lower median max value and adrenal gland area compared to those aged ≥40 years (<40 years: 1,004 *vs.* ≥40 years: 1,603, p<0.01 and <40 years: 478 mm^2 *vs.* ≥40 years: 834 mm^2, p=0.017, respectively).
Conclusion: Adrenal gland signal intensity and gland size on whole-body DWIBS are significantly higher in males than in females. In females, both signal intensity and adrenal area increase with age, suggesting age-related physiological or hormonal influences on adrenal gland characteristics.

Keywords: Adrenal signal, hydrogen atoms, body imaging with background body signal suppression, MRI/DWIBS, signal intensity.

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Received August 22, 2025 | Revised November 7, 2025 | Accepted November 12, 2025

Introduction

Magnetic resonance imaging (MRI) is a technique used to visualize the dynamics of hydrogen atoms in living organisms. Recently, whole-body diffusion-weighted imaging has been employed to perform comprehensive systemic examinations. In particular, diffusion weighted whole body imaging with background body signal suppression (DWIBS) enables imaging during free breathing. In this technique, the b-value in diffusion-weighted imaging is set high, typically between 800s/mm^2 to 1,000s/mm^2, to effectively suppress natural background signals from tissue (1). DWIBS is widely used in the diagnosis of malignant tumors that require whole-body examination.

Cancerous lesions, such as those found in breast cancer, exhibit high signal intensity in diffusion-weighted imaging because the free movement of water molecules is restricted (2). In the breast, malignant lesions generally have longer T1 relaxation times than benign lesions (3). The Short T Inversion Recovery (STIR) sequence suppresses signals from tissues with short T1 values, whereas tissues with long T1 values are less affected. Consequently, STIR may be particularly useful for detecting malignant tumors.

A comparative study between positron emission tomography (PET) using 18F-fluoro deoxy glucose (18F-FDG), a glucose analog, and DWIBS was conducted on 16 patients with malignant tumors (12 with lung cancer, two with colorectal cancer, one with breast cancer, and one with lung metastasis), comprising 27 lesions in total. DWIBS successfully identified 25/27 lesions, while PET detected 22/27 (4). However, image interpretation often involves not only DWIBS, but also complementary sequences, including whole-body diffusion-weighted, T1-weighted, T2-weighted, and fusion images acquired simultaneously.

One major challenge in image interpretation is the physiological variation in signal intensity among healthy organs. The adrenal glands, located above the kidneys and prone to distant metastasis, may also be affected by benign or unrelated conditions such as adenomas and hyperplasia, necessitating careful evaluation. Anatomically, the adrenal glands are divided into two regions: the adrenal medulla and the adrenal cortex, both of which play crucial roles in endocrine function. The medulla, located medially to the kidney, produces catecholamines such as adrenaline. The cortex, located peripherally, secretes several hormones, including cortisol, aldosterone, and dehydroepiandrosterone (5).

Despite advancements in imaging, several clinical questions remain unanswered: 1) Is there a difference in adrenal signal intensities between males and females in MRI imaging? and 2) does the adrenal signal intensity vary with age? This study aims to examine the influence of sex and aging on adrenal gland signal intensities in MRI.

Patients and Methods

Patient selection. This was a single-center, retrospective, patient-control study. Patients who underwent DWIBS for a health checkup, evaluation of elevated tumor markers, fever of unknown origin, or workup for a suspected tumor at Iga City General Hospital between April 2019 and April 2025, and in whom no malignant tumor was identified, were included in the study. Patients who did not provide consent to participate in the study, those with a history of malignant tumors, those suspected of having a malignant tumor on DWIBS, and patients with and bowel inflammation (acute diverticulitis) were excluded.

DWIBS examination. In this study, DWIBS imaging was performed using an Inginia 1.5T MRI system (Philips; Tokyo, Japan and Amsterdam, the Netherlands). The diffusion weighted imaging protocol was set as follows: repetition time (TR)=5,000 ms, echo time (TE)=66 ms, single-shot echo planar imaging (EPI), bandwidth=42.3 Hz, field of view (FOV)=460 mm (frequency)×316 mm (phase), matrix size=128×86, slice thickness=7 mm, voxel size=3.59×3.54 mm, number of excitations (NEX)=2, and parallel imaging with free-breathing acquisition. Three types of coils were used: a head and neck coil, a body coil, and an anterior coil. The body was divided into three regions for imaging. Two of the three coils were combined as appropriate for each region, and the final result was reconstructed as a single composite whole-body image.

Using the aforementioned MRI system, the following images were obtained: (1) a DWIBS maximum intensity projection (MIP) images; (2) transverse diffusion-weighted images, (3) transverse apparent diffusion coefficient (ADC) images, (4) coronary diffusion-weighted images, (5) coronary T1-weighted images, (6) coronary STIR images, (7) transverse in phase/out phase images, and (8) fusion images. These imaging methods collectively constitute the DWIBS examination in this study.

For image analysis, a radiation oncologist and nuclear medicine specialist (Y.O) with DWIBS imaging experience from 2016 manually set the region of interest (ROI) on the left adrenal gland on transverse diffusion-weighted images, referencing anatomical landmarks. The left adrenal gland was selected because the right adrenal gland often overlaps with the liver, which can interfere with accurate measurement. The maximum signal intensity across all slices of the left adrenal gland was recorded on the transverse diffusion-weighted images. In addition, the ROI was used to calculate the area (mm^2) of left adrenal gland.

In diffusion-weighted imaging, the signal intensity obtained without the application of a gradient field is defined as the b value (S_0), and the signal intensity after application is defined as the diffusion coefficient (D).

$$S = S_0 e^{-bD} \qquad (6)$$

One transverse ADC images, the maximum ADC (max ADC) signal intensity of the left adrenal gland was measured across all slices. The b value was set constant at 1,000 s/mm^2.

Image evaluation was performed using a reporting terminal system (PSP, Japan, Tokyo) and an RX660 monitor (EIZO, Ishikawa, Japan). On this monitor, pixel brightness corresponds directly to signal intensity; therefore, pixel brightness was used as the measured signal intensity in this study, particularly for whole body DWI image.

The ADC value is calculated by the following formula: ADC value=(Pixel value×0.0409225)×Real World Slope + (0.0409225×Real World Intercept).

In this system, numerical values are displayed without units. Therefore, in this study, the measured values were standardized and expressed relative to the conventional ADC scale.

Statistical analysis. Statistical analysis was performed using eZR, developed by the Omiya Medical Center of Jichi Medical University (7). Comparison between the two groups was made using the Mann-Whitney *U* test. Spearman's rank correlation coefficient was used to calculate the correlation coefficient. *p*-Values of <0.05 were considered statistically significant.

Ethical considerations and informed consent. This study was performed with the approval of the Ethics Committee of IGA City General Hospital (medical examination No. 344 and 564, DWIBS No. 92). An opt-out option was applied for all patients receiving regular medical examinations. The study's aims and procedures were explained to all health checkup patients, and a written informed consent to use data for the study was obtained. For patients whose data was collected up to March 2025, the opt-out procedure (No. 92) was implemented. For patients examined from April 2025 onward, written informed consent was directly obtained.

Results

Patients. Overall, 60 patients were included in this study. Six patients were excluded: two patients with a past history of cancer, one patient with prostate cancer, one patient with a suspected tumor, one patient with acute bowel inflammation and rheumatism, and one patient who did not consent. Among the participants, one female patient with polymyositis/dermatomyositis who was receiving steroid therapy was also included.

Comparison between male and female. A total of 22 male patients were analyzed, with a mean age of 58.2±11.7 years (median, 55 years). ADC images were not available for one male patient. The female group included 38 patients with a

Table I. *Patients' characteristics and results comparison between males and females.*

Factor	Male	Female
Number of patients	22	38
Age	58.2±11.7 years	55.9±15.4 years
Maximum value for the left adrenal in diffusion-weighted imaging	1,885.5±352.0	1,517.1±429.5.
Left adrenal gland area	1,198±435.0 mm^2	760.5±325.6 mm^2
Maximum ADC value for the left adrenal gland	2.02±0.26×10^{-3} mm^2/s	1.96±0.46×10^{-3} mm^2/s

ADC: Apparent diffusion coefficient.

mean age of 55.9±15.4 years (median=53.5 years), and ADC images were unavailable for two female patients. There was no statistically significant difference in age between males and females (p=0.447). In males, the maximum signal intensity of the left adrenal gland on diffusion-weighted imaging was 1,885.5±352.0, with a median value of 1,855. The mean area of the left adrenal gland was 1,198.0±435.0 mm^2, with a median of 1,159 mm^2. The maximum ADC value of the left adrenal gland was (2.02±0.26)×10^{-3} mm^2/s, with a median of 1.894×10^{-3} mm^2/s.

In females, the maximum signal intensity of the left adrenal gland on diffusion-weighted imaging was 1,517.1±429.5, with a median value of 1,472. The mean adrenal area was 760.5±325.6 mm^2, with a median of 768.5 mm^2. The maximum ADC value was (1.96±0.46)×10^{-3} mm^2/s, with a median of 2.012×10^{-3} mm^2/s. These results are summarized in Table I.

Comparison between males and females. The median values for max value of the left adrenal gland on diffusion-weighted imaging were significantly larger in male patients (males: 1,855 *vs.* females 1,472, p<0.01). The median values for adrenal gland area were significantly larger in male patients (males: 1,159 mm^2 *vs.* females: 768.5 mm^2, p<0.01, Figure 1 and Figure 2). In contrast, there was no significant difference in the maximum ADC value between sexes (p=0.774).

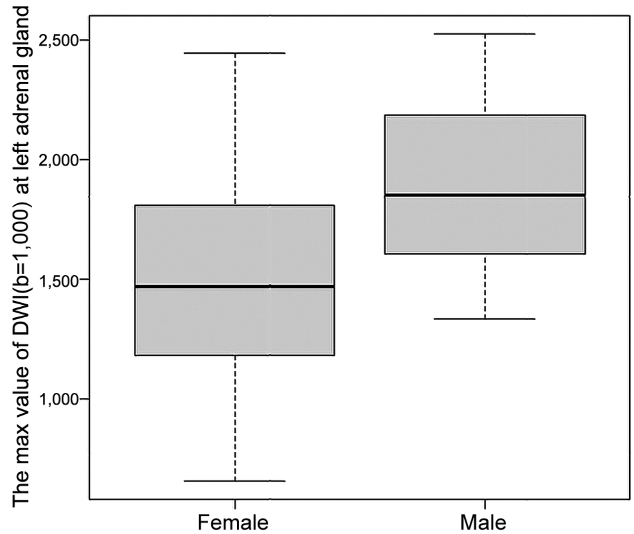

Figure 1. *Signal intensity values of the adrenal glands in diffusion-weighted imaging in males and females.*

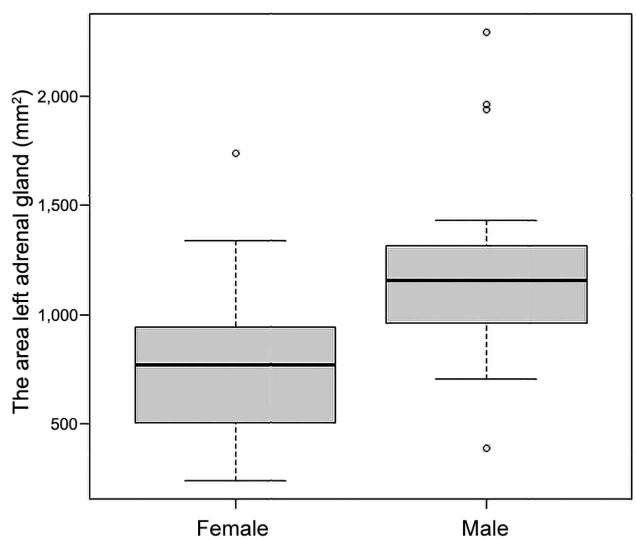

Figure 2. *Median value for the left adrenal gland area in males and females.*

Considerations in males. Among the 22 male patients, 12 were aged <60 years and 10 were aged ≥60 years. The median maximum diffusion-weighted imaging value for the left adrenal gland in diffusion-weighted imaging was 1,763.5 in patients aged <60 years and 1,859.5 in patients aged ≥60 years, showing no significant difference (p=0.674). The

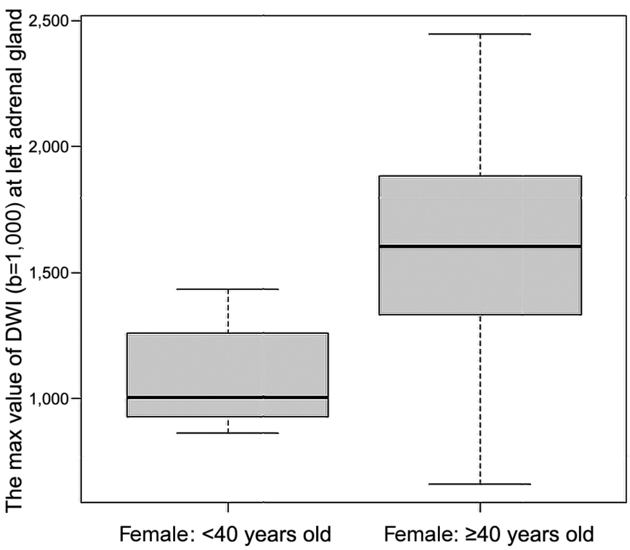

Figure 3. *The median max values of the left adrenal gland in diffusion-weighted imaging in patients aged <40 years and those aged ≥40 years.*

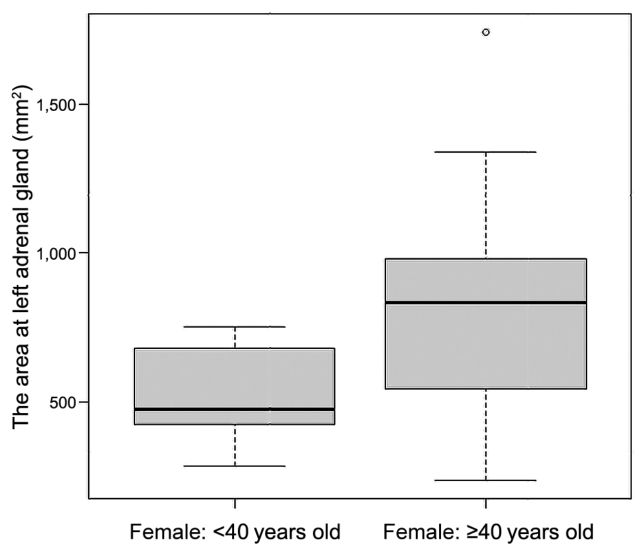

Figure 4. *The median values of the left adrenal gland area in diffusion-weighted imaging in patients aged <40 years and those aged ≥40 years.*

median adrenal gland area was 1,134.0 mm^2 in patients aged <60 years and 1,204.5 mm^2 in patients aged ≥60 years, also showing no significant difference (p=0.42). The median maximum ADC value was $2.04 \times 10^{-3} mm^2/s$ in patients aged <60 years and $1.86 \times 10^{-3} mm^2/s$ in patients aged ≥60 years, with no significant difference (p=0.57).

Considerations in females. Analysis at age 40. Seven female patients were aged <40 years and 31 were aged ≥40 years. The median maximum diffusion-weighted imaging value for the left adrenal gland was 1,004 for female patients <40 years and 1,603 for those aged ≥40 years, showing a significant difference (p<0.01, Figure 3). The median adrenal gland area was 478 mm^2 for those <40 years and 834 mm^2 for those aged ≥40 years, also showing a significant difference (p<0.01, Figure 4). The median maximum ADC value for the left adrenal gland area was $2.3 \times 10^{-3} mm^2/s$ for those aged <40 years and $2.0 \times 10^{-3} mm^2/s$ for those aged ≥40 years, showing a significant difference (p=0.038).

Analysis at age 50. Thirteen female patients were aged <50 years and 25 were aged ≥50 years. The median maximum diffusion-weighted imaging value for the left adrenal gland was 1,341 for female patients aged <50 years and 1,603 for those aged ≥50 years, showing a significant difference (p=0.025). The median value for the left adrenal gland area was 678 mm^2 for those <50 years and 814 mm^2 for patients aged ≥50 years, showing no significant difference (p=0.234). The median maximum ADC value was $2.1 \times 10^{-3} mm^2/s$ for patients <50 years and $2.0 \times 10^{-3} mm^2/s$ for those aged ≥50 years, showing no significant difference (p =0.165).

Analysis at age 60. Twenty-four female patients were aged <60 years and 14 aged ≥60 years. The median maximum diffusion-weighted imaging value for the left adrenal gland was 1,417 for female patients aged <60 years and 1,569 for those aged ≥60 years, showing no significant difference (p=0.273), The median value for the left adrenal gland area was 777 mm^2 for patients <60 years and 768.5 mm^2 for those aged ≥60 years, showing no significant difference (p=0.754). The median maximum ADC value was $2.0 \times 10^{-3} mm^2/s$ for patients <60 years and $2.1 \times 10^{-3} mm^2/s$ for those aged ≥ 60 years, showing no significant difference (p=0.960).

Correlations. In female patients, a statically significant positive correlation was observed between age and the

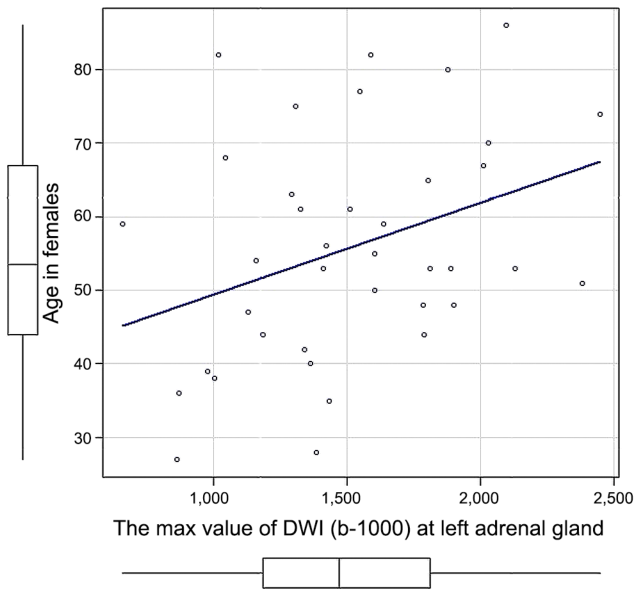

Figure 5. *Correlation between max value for the left adrenal gland on diffusion-weighted imaging and the age in females.*

maximum signal intensity (r=0.329, p=0.043, Figure 5). No significant correlation was found between age and the maximum ADC value (r=-0.211, p=0.223). A representative plot illustrating the relationship between the maximum DWI signal intensity and the adrenal gland area is shown in Figure 5.

Discussion

This study demonstrated that, in a non-cancer-bearing population, the maximum signal intensity of the left adrenal gland in diffusion-weighted imaging is significantly higher in males than in females. Moreover, the left adrenal gland area was also significantly larger in males compared to females. In female patients, the maximum diffusion-weighted imaging value increased in those aged ≥40 years and ≥50 years compared to younger age groups, indicating that signal intensity changes with age. Similarly, the left adrenal gland area and maximum ADC values were higher in woman aged ≥ 40 years, although the relationship between diffusion-weighted imaging intensity and adrenal gland area was not entirely consistent.

According to the formula (1), the diffusion-weighted imaging signal intensity depends on the initial intensity (T2 weighted image), the b-value, and the ADC value. In this study, the b-value was held constant, suggesting that the variations in signal intensity were primarily influenced by the initial T2 weighted signal and ADC. A previous research study including 32 patients reported ADC values of 1.44×10^{-3} mm^2/s in prepubertal subjects (age range=2.5 months-12 years; 4 males, 8 females), and in 1.23×10^{-3}mm^2/s in post-pubertal subjects (age range=11.9-60 years; 5 males, 15 females) (8). ADC values have also been shown to correlate positively with glomerular filtration rate in the kidney (9). However, in this study, there was no significant correlation between maximum diffusion-weighted imaging signal intensity and the maximum ADC value in either males or females, suggesting that the increased signal intensity cannot be attributed solely to diffusion.

Another possible contributor to the diffusion-weighted signal is the T2-weighted intensity itself, which forms the basis of the b=-0 s/mm^2 measurement. Catecholamine production in the adrenal medulla increases with age (10-13), and older adult males produce more than younger ones (11, 12). Despite this, diffusion-weighted imaging signal intensity of the left adrenal gland did not appear to directly reflect catecholamine production.

Hormones synthesis in the adrenal cortex occurs via cholesterol metabolism (14). In the zona glomerulosa, aldosterone is synthesized via pregnenolone and progesterone (14); in the zona fasciculata, cortisol is produced via pregnenolone and 17OH-pregnenolone; and in the zona reticularis, DHEA, a precursor of dehydroepiandrosterone sulfate and potentially of androstenedione (14), is produced via pregnenolone and 17OH-pregnenolone (14). Androstenedione is a precursor of testosterone and potentially of estrone (14). 17β-estriol is produced from testosterone and estrone. Cholesterol levels fluctuate with age and sex. In a previous study involving 30,802 males and 60,417 females aged 40-79 years with no history of cardiovascular disease, mean low-density lipoprotein (LDL) cholesterol levels were slightly higher in females (15). A 2017 Japanese Ministry of Health, Labour and Welfare survey reported that the total and LDL-C cholesterol levels in females begins to rise after menopause, surpassing levels in males after the age of 50, while cholesterol levels in males remain relatively stable until their 60s and 70s (16, 17).

Considering these findings, it is plausible that the increased signal intensity of the adrenal glands reflects cholesterol uptake by the adrenal cortex and its subsequent conversion to pregnenolone, rather than the levels of individual adrenal hormones. This hypothesis is supported by our observation that the left adrenal gland area was larger in males than females, and that younger females (<40 years) had smaller adrenal gland areas than older females, potentially indicating age- and menopause-related shifts in cholesterol metabolism and adrenal hormone synthesis.

Unlike PET-CT imaging, which can be affected by physiological stress during ^{18}F-FDG administration and lead to variable adrenal uptake (18-20), MRI, particularly DWIBS, is non-invasive and does not require contrast of radioactive tracers. Therefore, changes in adrenal signal intensity observed in DWIBS may more accurately reflect physiological function.

ADC values have been widely reported as useful quantitative indicators in oncology. Changes in ADC values are prognostic in locally advanced rectal cancer following chemoradiation therapy (21), predictive in 90Y-radioembolixation therapy (22), and used for staging in prostate cancer (23). These studies highlight the utility of ADC values as a quantitative measure; however, our results suggest that the diffusion-weighted image signal intensity itself may also serve as a valuable quantitative indicator of adrenal physiology.

Study limitations. First, it was retrospective in design. Second, the sample size was relatively small. Third, hormone levels and menopausal status were not directly evaluated, limiting the ability to correlate imaging findings with endocrine function. Future studies should prospectively investigate the relationship between adrenal diffusion-weighted imaging signal intensity, ADC values, and circulating hormone levels, including postmenopausal status, to better understand the physiological basis of adrenal imaging characteristics.

Conclusion

This study demonstrated that the maximum signal intensity of the left adrenal gland in whole-body diffusion-weighted imaging using DWIBS was significantly higher in males than females. In addition, age-related variation in adrenal signal intensity was observed among female patients.

Conflicts of Interest

Y.O. was a member of Expert Imaging and Interventional Support (EIIS), undertaking the medical imaging reading at Iga City General Hospital. All other Authors declare no conflicts of interest for this study.

Authors' Contributions

T.M.: conception (research idea), clinical data extraction; Y.O.: image data analysis; Y.U., S.S., H.F., H.S., K.T.: content check; S.W., M.N., H.U., K.T., T.G, K.Y, A.Z, D.H, A.N, C.K., M.U.: technical guidance concerning MRI.; K.S: final check and assessment concerning MRI.

Acknowledgements

We would like to express our gratitude to PSP Corporation and its employees for providing us with technical guidance.

Funding

No funding was used for this study.

Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine learning software, were used in the preparation, analysis, or presentation of this manuscript.

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