JPPIPA 9(7) (2023)

Jurnal Penelitian Pendidikan IPA

Journal of Research in Science Education

http://jppipa.unram.ac.id/index.php/jppipa/index

Analysis of Gray Matter Volume (GMV) and White Matter Hyperintensity (WMH) in Ischemic Stroke Patients with Fluid Attenuated Inversion Recovery (FLAIR) Imaging

Ade Lina Nur Fadlilah[1], Johan Andoyo Effendi Noor[1*], Yuyun Yueniwati[2,3], Karimah[1]

[1] Department of Physics, Universitas Brawijaya, Malang, Indonesia.
[2] Department of Radiology, Universitas Brawijaya, Malang, Indonesia.
[3] Department of Radiology, Universitas Islam Negeri Maulana Malik Ibrahim, Malang, Indonesia.

Received: March 8, 2023
Revised: June 1, 2023
Accepted: July 25, 2023
Published: July 31, 2023

Corresponding Author:
Johan Andoyo Effendi Noor
jnoor@ub.ac.id

DOI: 10.29303/jppipa.v9i7.3377

Abstract: Stroke is a serious health problem faced by almost all over the world. The occurrence of ischemic stroke could affect the gray matter volume (GMV) in the human brain. In Magnetic Resonance imaging of an ischemic stroke with a FLAIR sequence, a white lesion known as the white matter hyperintensity (WMH) is often found. We studied correlation between gray matter volume (GMV) and white matter hyperintensity (WMH) in ischemic stroke patients using fluid attenuated inversion recovery (FLAIR) sequences. The MRI data were taken randomly from ten ischemic stroke patients (mean age 46.9 years) and ten normal patients (mean age 36.8 years). FLAIR axial image parameters, i.e. TE (time echo), TR (time repetition), and TI (time inversion) were analyzed. The results reveal that the TE and TR values in FLAIR images of normal and ischemic stroke patients are classified as long TE (more than 70 ms), long TR (more than 1500 ms) and long TI (more than 1700 ms). The mean GMV of ischemic stroke patients (1.371 cm^3) is smaller than the GMV of normal patients (2.267 cm^3). This is related to the presence of white matter hyperintensity (WMH) in ischemic stroke patients.

Keywords: FLAIR; Gray matter volume; Hyperintensity; Magnetic resonance imaging; White matter

Introduction

A stroke is the sudden death of several brain cells due to lack of oxygen when blood flow to the brain is cut off due to a blockage or rupture of blood vessels in the brain. Based on WHO data for 2019, stroke is one of the most common causes of global death in the world (Phipps & Cronin, 2020; WHO, 2020). Over the last few decades, the incidence of stroke has decreased by 42% in developed countries, but the incidents are more than doubled in developing countries (Kemenkes Republik Indonesia, 2019).

Based on the anatomic pathology and its causes, stroke is divided into two types, i.e. ischemic stroke and hemorrhagic stroke. The ischemic stroke is more common than the hemorrhagic stroke (Yueniwati, 2016), where the highest incidence rate in Indonesia reaches 83% (Badan Penelitian dan Pengembangan Kemenkes RI, 2018). Ischemic stroke is a blockage of blood vessels that causes blood flow to the brain to stop partially or completely (Brown, 2023). Blockage in ischemic stroke can occur along the arteries leading to the brain (Yueniwati, 2016). The occurrence of ischemic stroke can affect the content of gray matter (gray matter) in the brain (Alam, 2020).

Gray matter volume (GMV), or what can be interpreted as gray matter volume, a quadratic function of distances in the surfaces and a linear function of the thickness (Alam, 2020). The brain consists of two types of tissue, i.e. white matter and gray matter (Mackenzie, 2023). Gray matter (GM) is composed of unmyelinated nerve cell bodies and axons. It forms the outermost layer

How to Cite:
Fadlilah, A. L. N., Noor, J. A. E., Yueniwati, Y., & Karimah. (2023). Analysis of Gray Matter Volume (GMV) and White Matter Hyperintensity (WMH) in Ischemic Stroke Patients with Fluid Attenuated Inversion Recovery (FLAIR) Imaging. *Jurnal Penelitian Pendidikan IPA*, *9*(7), 5031–5038. https://doi.org/10.29303/jppipa.v9i7.3377

of the brain and is pinkish-gray in color, therefore it is called gray matter (Mercadante & Tadi, 2022).

Gray matter is a major component of the central nervous system which has an important role in processing information in the brain. Structures in the gray matter signal from sensory organs or other areas of the gray matter. This network directs sensory stimuli to neurons in the central nervous system where synapses induce responses to stimuli (Mercadante & Tadi, 2022).

One of the stroke diagnostic methods currently being developed is imaging using the magnetic resonance imaging (MRI), a technique for taking images of organs using the principle of magnetic resonance of the hydrogen atomic nucleus of the organs. The scanner in an MRI uses a strong magnetic field, a magnetic field gradient, and radio waves to produce images of organs inside the body (McRobbie, 2020; Yueniwati, 2016).

The basic principle of MRI is based on the magnetic resonance of the nucleus together with the relaxation of the proton spins in the nucleus. Under normal circumstances without any disturbance, the protons in the molecules of the human body's tissues have spins in random directions (Powers, 2021). If the proton is subjected to a very strong external magnetic field, the direction of the proton spins will be parallel or opposite (anti-parallel) to the direction of the external magnetic field (Grover et al., 2015).

If the proton is given an electromagnetic wave in the form of a radio frequency (RF) signal, there will be a change from the spin equilibrium and absorption of electromagnetic energy by the atomic nucleus will occur, which is called excitation. If the RF signal is turned off, the proton nucleus will relax back in its original direction. The relaxation of the proton nucleus is divided into two parts, i.e. longitudinal relaxation, and transverse relaxation (Kwok, 2022; Grover et al., 2015).

Longitudinal relaxation occurs due to energy exchange between the spin and lattice so it is called spin-lattice relaxation (Powers, 2021). The lattice spin interaction that occurs starts with a spin that comes from high energy and returns to low energy so that the RF energy will be released back into the lattice around it. This longitudinal magnetization recovery process occurs in time T1, where T1 is the time required to recover 63% of the longitudinal magnetization after an RF pulse of 90^{o} (Powers, 2021; Grover et al., 2015).

When relaxation occurs, where initially the maximum RF signal is then stopped and the signal is lost, then the spins will go out of phase which was originally uniform to become non-uniform. The interaction between these spins is known as transverse relaxation. The time required for this transverse relaxation process is known as T2 (Kiselev & Novikov, 2018).

In short, scanning an image with an MRI is done by sending a radio frequency signal that will disturb the magnetic moment of the hydrogen atom nucleus in the body. Changing the magnetic gradient requires a program called a pulse sequence(Wardlaw et al., 2015). Various sequences in MRI can be used in brain imaging processes, one of which is fluid-attenuated inversion recovery (FLAIR) (Moghadam et al., 2017).

FLAIR is a sequence based on T2 weights. The FLAIR technique was developed in the early 1990s by a team of Hammersmith Hospital researchers led by Graemme and coworkers (Ahmed Mesrur & David Mark, 2018). FLAIR sequences produce diagnostic images from T2 weights by excluding the signal intensity of the cerebrospinal fluid which is characterized using a long Time Inversion (TI) and Time Echo (TE). The FLAIR technique is proven capable of scanning various diseases using an MRI machine (Moghadam et al., 2017).

Recent research conducted by Galie et al. (2020) stated that gray matter can also be observed using Fluid Attenuated Inversion Recovery (FLAIR) sequences. In addition, a very common finding when observing the brain with MRI imaging using FLAIR sequences in elderly subjects and patients who have had a stroke is White Matter Hyperintensity (WMH). Wardlaw et al. (2015) conducted a study on the origin of the appearance of WMH using CTScan and MRI imaging modalities. WMH was commonly found in the elderly, and initially, this WMH finding was considered a normal finding with increasing age (Merino, 2019). However, further study proved that WMH findings are often an indication of the occurrence of a disease, one of which is in ischemic stroke patients (Cho et al., 2015).

Method

Subjects in this study were ischemic stroke patients and normal patients (as the control population). The materials used in this study were 10 axial Fluid Attenuated Inversion Recovery (FLAIR) images of ischemic stroke patients ranging in age from 8 to 65 years and 10 axial FLAIR images of normal patients ranging in age from 7 to 77 years sent to the Radiology Department of a General Public Hospital in Malang, East Java, Indonesia. The images were produced by the Magnetic Resonance Imaging (MRI) 3.0 T. The RadiAnt Dicom Viewer software was utilized to inspect the images, and ImageJ software to analyze them.

The targets to be achieved in this study are long-time echo (TI), time repetition (TR), and time inversion (TI) intervals with a TE range of 140 ms, a TR of around 8000 ms, and a TI ranging from 2000 to 2500 ms. The next target is to obtain GMV atrophy and increased white

matter hyperintensity (WMH) volume in ischemic stroke patients. In addition, there was also a greater increase in GMV and WMH atrophy in the brain images of patients with ischemic stroke compared to the brain images of a normal patient.

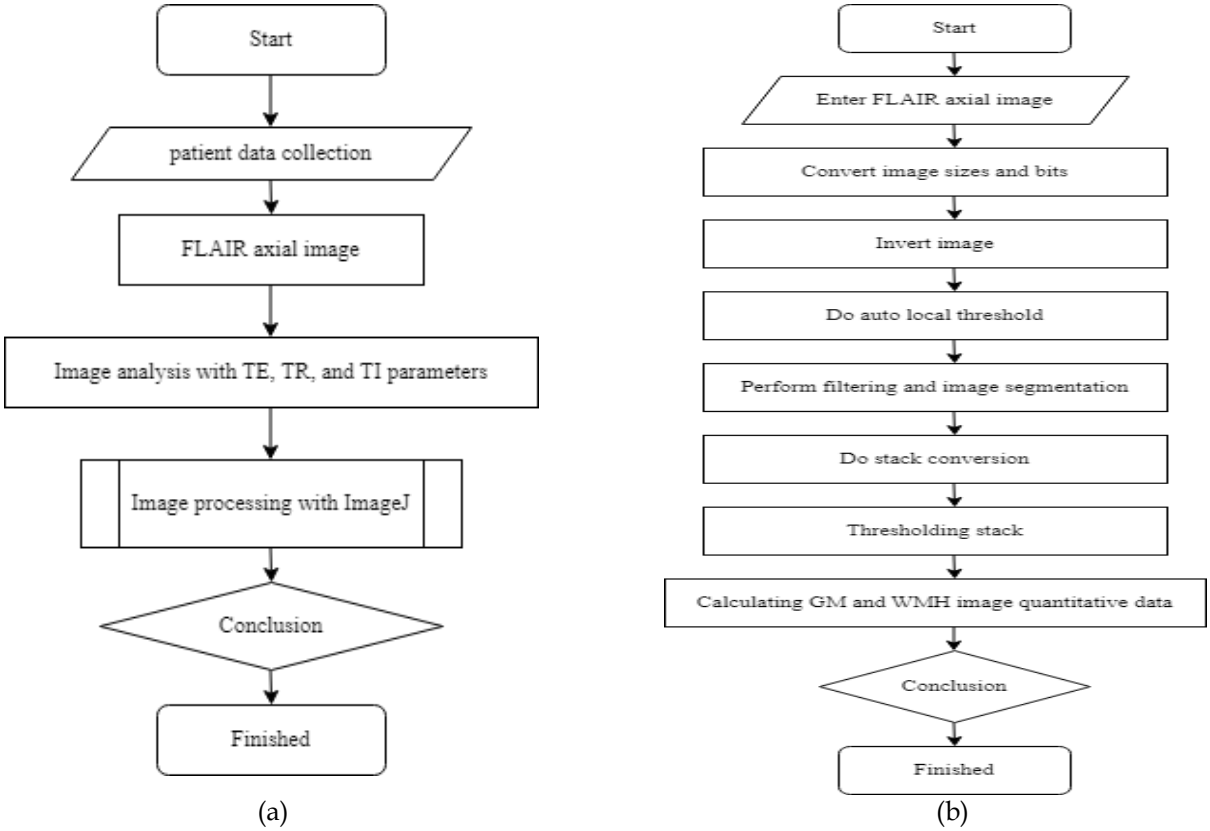


Figure 1. Flowchart (a) image capture stage with MRI (b) stages of image processing with ImageJ

Figure 1 is the flowchart of the research. Figure 1 (a) is the procedure of image capture and Figure 1 (b) is the procedure of image processing using ImageJ.

Result and Discussion

Data on TE, TR, and TI values in each ischemic stroke patient and normal patient are presented in Tables 1 and 2. In these tables, the time echo (TE) values in patient images are classified as "long TE" because almost all images of ischemic and normal patients have values greater than 70 ms (Setiawan et al., 2016). Long TE values are needed to produce good T2-weighted images. The longer the TE value, the longer the protons' transverse relaxation, resulting in more signal decay. A lot of signal decay results in less signal intensity being generated. This low signal intensity will appear dark on MRI imaging. So it can be concluded that a small signal intensity will minimize the process and produce the desired image (Setiawan et al., 2016).

The repetition time (TR) value in all patients was greater than 1500 ms, so the TR value in patients was classified as "long TR" (IMAIOS SAS, 2022). With a long TR resulting in a magnetization process in the direction of equilibrium ($\mathbf{M_z}$) or longitudinal relaxation for all types of tissues such as CSF, white matter, gray matter, and fat, the magnetization has reached its maximum. When all these networks have reached their maximum magnetization, the difference in relative signal intensity for all networks, as mentioned above, becomes insignificant due to the reduced T1 value of each network.

Long TE and TR values produce images with a T2 weight. T2 image weighting is often used to observe pathological abnormalities. However, in brain tissue, the high CSF signal needs to be removed to observe brain abnormalities more clearly. The technique that can be used to achieve this goal is to use the Fluid-Attenuated Inversion Recovery (FLAIR) sequences. FLAIR sequences can be performed using long-time inversion (TI), with values greater than 1700 ms (Lutvia, 2016).

In the data, the TI values in normal and ischemic patients are more than 1700 ms, so the TI value can be classified as a long TI. Long TI values will reduce the relative signal intensity of CSF and tissue with relatively equal T1 and T2 values so that they will appear darker (hyperintense). Since the CSF and these tissues appear hyperintense, there will be a different signal from a

WMH lesion. The difference in the signal from these lesions makes WMH appear clearer, so it is easier to observe (Wardlaw et al., 2015). However, this causes the gray matter and white matter networks to have almost the same signal, so that the two images appear to have almost the same color, although differences can still be observed between the two.

Table 1. Data of TE, TR, and TI Parameters from Images of Ischemic Stroke Patients

Patient Index	Age (y.o.)	Parameter Value (ms)		
		Time Echo	Time Repetition	Time Inversion
S1	8	120	11000	2800
S2	32	340	4800	1650
S3	35	340	4800	1650
S4	36	87.28	9000	2572.03
S5	48	120	11000	2800
S6	60	111.61	12000	2850
S7	61	340	4800	1650
S8	62	120	11000	2800
S9	62	120	11000	2800
S10	65	100	11000	2800

Table 2. Data of TE, TR, and TI Parameters from Normal Patients

Patient Index	Age (y.o.)	Parameter Value (ms)		
		Time Echo	Time Repetition	Time Inversion
N1	7	325.06	4800	1650
N2	10	325.90	4800	1650
N3	19	85.82	9000	2567.07
N4	27	340	4800	1650
N5	40	86.54	9000	2569.85
N6	47	90.56	9000	2571.24
N7	59	336.77	4800	1650
N8	16	78	9000	2500
N9	66	78	9000	2500
N10	77	92	8000	2370

Table 3. Slice Thickness Values of Normal Patients (N) and Ischemic Stroke Patients (S)

Patient Index	Slice Thickness (mm)	Patient Index	Slice Thickness (mm)
N1	1.5	S1	5
N2	5	S2	5
N3	5	S3	5
N4	5	S4	5
N5	5	S5	5
N6	5	S6	5
N7	1.5	S7	5
N8	5	S8	5
N9	5	S9	5
N10	5	S10	5

Table 4. Results of Calculating GMV and WMH Values in Stroke Patients (S)

Patient Index	Age (y.o)	GMV (cm^3)	WMH (cm^3)
S1	8	1.10	0.05
S2	32	2.22	0.00
S3	35	3.17	0.08
S4	36	1.70	0.00
S5	48	1.05	2.57
S6	60	0.25	0.04
S7	61	2.45	0.12
S8	62	0.53	0.38
S9	62	0.83	0.78
S10	65	0.40	0.11
Average		1.37	0.41

Table 5. Results of Calculating GMV and WMH Values in Normal Patients

Patient Index	Age (y.o)	GMV (cm^3)	WMH (cm^3)
N1	7	0.27	0.00
N2	10	7.63	0.00
N3	19	2.25	0.00
N4	27	4.31	0.00
N5	40	2.51	0.00
N6	47	2.32	0.00
N7	59	0.24	0.05
N8	16	0.85	0.00
N9	66	0.95	0.01
N10	77	0.95	0.28
Average		2.27	0.04

The next step is the image processing stage using ImageJ so that the gray matter (GM) and white matter hyperintensity (WMH) area values are obtained. After obtaining quantitative data in the form of the area of gray matter and WMH, calculations can then be carried out to calculate the volume of both. To calculate the volume of GM and WMH, the area obtained can be multiplied by the slice thickness of each patient. Slice thickness values for each patient can be seen in the RadiAnt Dicom Viewer software. Slice thickness for each patient are presented in Table 3. Then the volume values of gray and white matters hyperintensities were calculated for each patient to obtain the values presented in Tables 4 and 5.

The patients in this study were divided into two groups, i.e. normal patients with the *N* index and ischemic stroke patients with the *S* index. Based on Tables 4 and 5, these patients can be classified into 8 age groups according to the age category division issued by the Indonesian Ministry of Health in 2009 (Amin, 2017) as follows:

Childhood, ages 5–11 (N1, N2, and S1). In this age group, the GMV of patients N1 is smaller than that of patients N2 and S1 because the slice thickness value of N1 (1.5 mm) is smaller than that of N2 and S1 (5 mm). In this age category, the GMV in normal patients is greater than the GMV in stroke patients. WMH was not found in normal patients, but it was found in stroke patients.

Early adolescents, aged 12–16 years (N8). In this age category, it is not possible to compare the GMV of normal patients and ischemic stroke patients because data on ischemic stroke patients at this age are not available. In the data of patients in this age category, WMH was not found.

Late adolescence, aged 17–25 years (N3). In this age category, data on ischemic stroke patients are also not available, so the GMV of ischemic stroke patients cannot be compared with that of normal patients. In this age category, WMH was not found.

Early adulthood, aged 26–35 years (N4, S2, and S3). GMV in patient N4 was greater than GMV in patients S2 and S3, with the same slice thickness in all three patients (5 mm). In this category, WMH was only found in patients with S3, while in patients N4 and S2, there was no WMH.

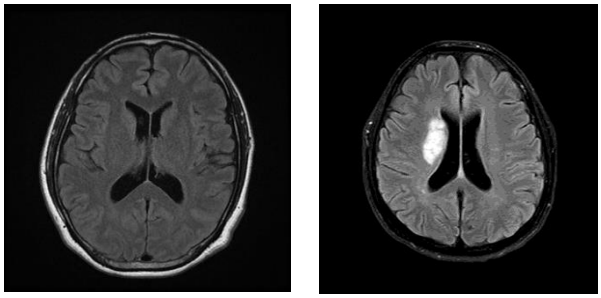
Late Adult, aged 36–45 years (N5 and S4). GMV in patient N5 is greater than GMV in patient S4, with the same slice thickness in both patients. In these two patients, no WMH was found in either patient.

Elderly 46-55 years old (N6 and S5). The GMV in N6 patients was greater than in S5 patients, with the same slice thickness in both patients. WMH was found in patient S5, while in inpatient N6 there was no WMH.

Late Elderly Age (56–65 years) (N7, S6, S7, S8, S9, and S10) The order of GMV from largest to smallest in this patient category is S7, S9, S8, S10, S6, and N7. Patient N7 had the smallest GMV because his slice thickness (1.5 mm) was smaller than the slice thickness of the other patients (5 mm). WMH was found in all patients in this age category, with the order of smallest to largest being S6, N7, S10, S7, S8, and S9.

For People over the age of 65 (N9 and N10). GMV in patient N9 was greater than that in patient N10, while WMH was found in both patients, with WMH in patient N10 being greater than WMH in patient N9, where the age of patient N10 (77 years) was older than the age of patient N9 (65 years). However, this age category cannot be compared with normal patients because data on normal patients in this age category are not available.

From the patient data, if they are averaged without considering the patient's age, the average GMV in normal patients is greater than the average GMV in ischemic stroke patients. The difference in GMV between normal patients and ischemic stroke patients is due to changes that occur in the GMV of ischemic stroke patients (Diao et al., 2017). This is related to the presence of lesions in the white matter of ischemic stroke patients, as shown in Figure 2. These lesions are known as white matter hyperintensities (WMH). The increase in WMH volume is associated with a decrease in GMV in ischemic stroke patients, resulting in a greater GMV in normal patients than in ischemic stroke patients.



(a) (b)

Figure 2. Illustration of a patient in the early stages of dementia. (a) Image of patient N6 (47 years) without white matter hyperintensity (WMH), (b) image of patient S5 (48 years old) with white matter hyperintensity (WMH)

From the data in Table 5, in the sample of normal patients, 3 patients found WMH in their images, e.g., patients with index numbers N7 (59 years), N9 (66 years), and N10 (77 years). All three patients were over 50 years old. Finding WMH at this age is reasonable because WMH is common at the age of 45 (Indrawati et al., 2016). Whereas in ischemic stroke patients, WMH was found in 8 out of 10 patients analyzed. Apart from individuals aged 45 years, WMH is also commonly found in stroke patients. According to Cho et al. (2015), there are changes in the pattern of white matter in stroke patients from time to time. WMH findings in stroke patients indicate how severe the changes are in the white matter of stroke patients. One of the signs of a normal aging process in humans is a reduced GMV in the brain (Cho et al., 2015). Reduced GMV is also a result of brain atrophy. One of the causes of brain atrophy is stroke. In stroke patients, there is an interruption of blood flow to parts of the brain that will affect the white matter and gray matter in the brain. The effect that is most often found in gray matter is reduced volume. Another sign that is commonly found in stroke patients is the presence of white matter hyperintensity (WMH) in the patient's main image taken using an MRI modality with FLAIR sequences. Imaging with the FLAIR sequence is very good at showing tissue abnormalities, one of which is the presence of WMH findings in normal elderly and elderly stroke patients. However, the FLAIR sequence is not good for observing a decrease in GMV. The analysis carried out in this study was assisted by the ImageJ software. ImageJ software has the advantage of converting qualitative data in the form of images into quantitative data. This analysis is needed to measure the volume of gray matter and white matter hyperintensities in patients so that data can be obtained, as was the case in the previous table. In GMV measurements, the process of filtering gray matter images is more difficult than when measuring WMH. This happens because the gray matter image in the FLAIR sequence looks faint and almost the same as the white matter image due to its low contrast, which affects the image processing process. It is different from the WMH filter process, where the software can easily analyze WMH images because the WMH contrast display is very clear, making the filter process performed by the software easier.

Conclusion

We can conclude that the time echo (TE) and time repetition (TR) values in FLAIR images of normal and ischemic stroke patients are classified as "long TE" and "long TR," with TE values of more than 70 ms and TR values of more than 1500 ms, respectively. The value of time inversion (TI) in all patients is also classified as a long TI with a TI value of more than 1700 ms. The average GMV of ischemic stroke patients (1.371 cm^3) is smaller than the GMV of normal patients (2.267 cm^3). This is related to the presence of white matter hyperintensity (WMH) in ischemic stroke patients.

Acknowledgments
The authors would like to express their gratitude to the Laboratory Assistants of Biophysics Laboratory, Physics Department, Brawijaya University for assisting us in conducting this research.

Author Contributions
Conceptualization, Johan A. E. Noor and Ade Lina Nur Fadlilah; methodology, Johan A. E. Noor and Ade Lina Nur Fadlilah; software, Ade Lina Nur Fadlilah; validation, Johan A. E. Noor and Yuyun Yueniwati; formal analysis, Ade Lina Nur Fadlilah and Johan A. E. Noor; investigation, Ade Lina Nur Fadlilah; resources, Ade Lina Nur Fadlilah, Johan A. E. Noor, and Yuyun Yueniwati; data curation, Johan A. E. Noor; writing—original draft preparation, Ade Lina Nur Fadlilah; writing—review and editing, Johan A. E. Noor; visualization, Ade Lina Nur Fadlilah; supervision, , Johan A. E. Noor and Yuyun Yueniwati; project administration, Karimah and Ade Lina Nur Fadlilah; funding acquisition, NaN. All authors have read and agreed to the published version of the manuscript.

Funding
This research received no external funding.

Conflicts of Interest
The authors declare no conflict of interest.

References

Ahmed Mesrur, H., & David Mark, Y. (2018). Susceptibility Weighted Imaging: Clinical Applications And Future Directions. *World Journal Of Radiology*, *10*(4). Https://Doi.Org/10.4329/Wjr.V10.I4.30

Alam, D. Y. (2020). *Analisis Grey Matter Volume Pada Pasien Stroke Iskemik Dengan Diffusion Weighted Magnetic Resonance Imaging Tesis*. Universitas

Brawijaya.

Amin, M. A. (2017). *K*lasifikasi Kelompok Umur Manusia Berdasarkan Analisis Dimensi Fraktal Box Counting Dari Citra Wajah Dengan Deteksi Tepi Canny. *MATHunesa: Jurnal Ilmiah Matematika, 5*(2). Retrieved from https://ejournal.unesa.ac.id/index.php/mathunesa/article/view/19398

Badan Penelitian Dan Pengembangan KEMENKES RI. (2018). *Hasil Riskesdas Tahun 2018* (P. 220) [Siwabessy_02112018]. Kementrian Kesehatan RI. Retrieved from https://kesmas.kemkes.go.id/assets/upload/dir_519d41d8cd98f00/files/hasil-riskesdas-2018_1274.pdf

Brown, R. (2023). *Stroke – Symptoms And Causes*. Mayo Clinic. Retrieved from https://www.mayoclinic.org/diseases-conditions/stroke/symptoms-causes/syc-20350113

Cho, A.-H., Kim, H.-R., Kim, W., & Yang, D. W. (2015). White Matter Hyperintensity In Ischemic Stroke Patients: It May Regress Over Time. *Journal Of Stroke*, *17*(1), 60. https://doi.org/10.5853/jos.2015.17.1.60

Diao, Q., Liu, J., Wang, C., Cao, C., Guo, J., Han, T., Cheng, J., Zhang, X., & Yu, C. (2017). Gray Matter Volume Changes In Chronic Subcortical Stroke: A Cross-Sectional Study. *Neuroimage: Clinical*, *14*, 679–684. https://doi.org/10.1016/j.nicl.2017.01.031

Grover, V. P. B., Tognarelli, J. M., Crossey, M. M. E., Cox, I. J., Taylor-Robinson, S. D., & Mcphail, M. J. W. (2015). Magnetic Resonance Imaging: Principles And Techniques: Lessons For Clinicians. *Journal Of Clinical And Experimental Hepatology*, *5*(3), 246. https://doi.org/10.1016/j.jceh.2015.08.001

IMAIOS SAS. (2022). *NMR Signal And MRI Contrast: Signal Weighting And Sequences Parameters | E-MRI*. IMAIOS. Retrieved from https://www.imaios.com/en/e-mri/nmr-signal-and-mri-contrast/signal-weighting-and-sequences-parameters

Indrawati, L., Sari, W., & Dewi, C. S. (2016). *Stroke, Cegah Dan Obati Sendiri* (1st Ed.). Penebar Plus.

Kemenkes Republik Indonesia. (2019). *Hari Stroke Sedunia 2019: Otak Sehat, SDM Unggul*. Direktorat P2PTM. Retrieved from http://p2ptm.kemkes.go.id/artikel-sehat/hari-stroke-sedunia-2019-otak-sehat-sdm-unggul

Kiselev, V. G., & Novikov, D. S. (2018). Transverse NMR Relaxation In Biological Tissues. *Neuroimage*, *182*, 149–168. https://doi.org/10.1016/j.neuroimage.2018.06.002

Kwok, W. E. (2022). Basic Principles Of And Practical Guide To Clinical MRI Radiofrequency Coils. *Radiographics*. https://doi.org/10.1148/rg.210110

Lutvia, H. (2016). *Pengaruh Variasi Waktu Pembalik (Time Inversion) Terhadap Citra Coronal Studi Pemeriksaan MRI Kepala* [Universitas Airlangga]. Retrieved from https://repository.unair.ac.id/54178/13/mpf_15-16_lut_p.pdf

Mackenzie, R. (2023, February). *Gray Matter Vs White Matter*. Neuroscience From Technology Networks. Retrieved from http://www.technologynetworks.com/neuroscience/articles/gray-matter-vs-white-matter-322973

Mcrobbie, D. W. (2020). *Essentials Of MRI Safety*. John Wiley & Sons.

Mercadante, A. A., & Tadi, P. (2022). Neuroanatomy, Gray Matter. In *Statpearls [Internet]*. Statpearls Publishing. Retrieved from https://www.ncbi.nlm.nih.gov/books/nbk553239/

Merino, J. G. (2019). White Matter Hyperintensities On Magnetic Resonance Imaging: What Is A Clinician To Do? *Mayo Clinic Proceedings*, *94*(3), 380–382. https://doi.org/10.1016/j.mayocp.2019.01.016

Moghadam R, N., Rahimdel, A., Shanbehzadeh, T., & Fallah, R. (2017). Comparison Of Diffuse Weighted Imaging And Fluid Attenuation Inversion Recovery Sequences Of MRI In Brain Multiple Sclerosis Plaques Detection. *Iranjchildneurol*, *11*, 8. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5329755/

Phipps, M. S., & Cronin, C. A. (2020). Management Of Acute Ischemic Stroke. *BMJ*, *368*. https://doi.org/10.1136/bmj.l6983

Powers, S. J. (2021). *MRI Physics: Tech To Tech Explanations*. John Wiley & Sons.

Setiawan, A. N., Suroso, A., & Rosyid. (2016). Pengaruh Variasi Time Echo (Te) Terhadap Citra Fluid-Attenuated Inversion Recovery (FLAIR) MRI Otak. Semarang: Prodi DIV T. Radiodiagnostik dan Radioterapi Semarang Poltekkes Kemenkes Semarang. Retrieved from https://www.researchgate.net/publication/322095397_pengaruh_variasi_time_echo_te_terhadap_citra_fluid-attenuated_inversion_recovery_flair_mri_otak/citations

Wardlaw, J. M., Hernandez, M., & Munos Maniaga, S. (2015). What Are White Matter Hyperintensities Made Of? Relevance To Vascular Cognitive Impairment. *Journal Of The American Heart*

Association, *4*(6), 19. https://doi.org/10.1161/jaha.114.001140

WHO. (2020). *The Top 10 Causes Of Death*. World Health Organization. Retrieved from https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death

Yueniwati, Y. (2016). *Pencitraan Pada Stroke* (1st Ed.). Universitas Brawijaya Press.