

# Advances in Machine Learning for Magnetic Resonance Imaging of Acute Ischemic Stroke: A Systematic Review

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## Abstract

Stroke demands rapid and precise diagnosis. Recent advancements in machine learning (ML) have facilitated its integration with magnetic resonance imaging (MRI) for assessing acute ischemic stroke (AIS). This systematic review delves into the utilization of ML algorithms in MRI-based AIS diagnosis and prediction, highlighting their prospective clinical implementation.

This systematic review followed PRISMA guidelines, conducting a thorough search across PubMed, Web of Science, Scopus, and Google Scholar. Inclusion criteria focused on studies predicting acute stroke onset time and identifying acute ischemic stroke within the therapeutic window using MRI data for AI algorithms. Only studies post January 1, 2018, were included. Excluded were studies involving chronic stroke patients, computed tomography (CT) scans, other imaging modalities, or lacking AI components.

Twelve articles met the criteria, primarily aiming to predict tissue status or ischemic core using deep learning techniques like CNNs, U-Nets, autoencoders, and GANs, often with attention mechanisms or pretrained networks. Magnetic resonance imaging modalities included ADC, DWI, FLAIR, and T2W, with some using advanced techniques like PWI and pCASL. Model performances varied, with some achieving high accuracy in identifying patients within treatment windows and segmenting ischemic regions. One study generated synthetic MRI data, while another accelerated MRI acquisition.

Machine learning algorithms exhibit promise in MRI-based AIS diagnosis and prediction, especially in segmenting ischemic regions and classifying patients for treatment. However, validation on larger and diverse cohorts is essential for robustness. Integrating ML techniques into MRI protocols could enhance AIS diagnosis and treatment planning efficiency and accuracy in the future.

**Keywords:** Machine learning, MRI, stroke

## INTRODUCTION

Stroke is a serious health issue that has significant impacts on individuals, communities, and economies worldwide.<sup>1</sup> It results in disabilities and death, and it also imposes a substantial economic burden, with estimated costs reaching approximately 34 billion dollars each year.<sup>2,3</sup> There are 2 primary types of stroke, which are ischemic stroke and hemorrhagic stroke. Ischemic stroke is the more common type, accounting for approximately 87% of all stroke cases. Ischemic stroke occurs when there is a blockage or clot in a blood vessel that supplies blood to the brain, leading to a lack of oxygen and nutrients, and ultimately causing damage to the brain tissue. Hemorrhagic stroke, on the other hand, occurs when there is bleeding in the brain due to a ruptured blood vessel. Both types of stroke can have severe consequences and require prompt medical attention.<sup>3</sup> During an acute ischemic stroke (AIS), there are 2 distinct areas of the brain that are affected: the penumbra and the infarction core. The penumbra is a region surrounding the infarction core that is considered reversible, meaning that brain cells in this area can still recover if blood flow is restored promptly. The infarction core, on the other hand, is an irreversible ischemic area, where brain cells have already been damaged due to the lack of oxygen and nutrients. The American Heart Association/American Stroke Association (AHA/ASA) recommends 2 primary treatment options for restoring blood flow in AIS, which are thrombolysis with tissue plasminogen activator (tPA) administered either intra-arterially or intravenously, and mechanical thrombectomy, also known as clot retraction.<sup>4</sup> Mechanical thrombectomy is considered the gold standard for the treatment of large vessel occlusions in acute ischemic stroke.<sup>5</sup> However, both tPA thrombolysis and mechanical thrombectomy are time-sensitive procedures that are typically performed within specific time windows after the onset of stroke. Tissue plasminogen activator thrombolysis is usually done within 4.5 hours from the onset of stroke, while mechanical thrombectomy is typically performed within 6 hours from the onset of stroke.<sup>6</sup> The importance of timely intervention in acute ischemic stroke cannot be overstated, as theoretical calculations suggest that every 1.6 minutes saved from the onset time of stroke could potentially spare approximately 3.1 million neurons from damage or death, leading to improved outcomes.<sup>7</sup> Recent prospective randomized studies, such as the DAWN study<sup>8</sup> and the DEFUSE-3<sup>5</sup> study, have expanded the treatment window for endovascular intervention in acute ischemic stroke cases, with the DAWN study showing that intervention can be extended up to 24 hours from the onset of stroke, and

the DEFUSE-3 study demonstrating the safety of intervention up to 16 hours.<sup>5,9,10</sup>

One challenge in treating AIS is determining the exact time of stroke onset, particularly for patients who experience a stroke during their sleep or unwitnessed strokes, known as wake-up stroke (WUS), which accounts for a significant portion of acute ischemic stroke cases.<sup>11</sup> Wake-up stroke patients have traditionally been excluded from treatment due to the inability to accurately ascertain the time of stroke onset. However, the “Wake Up Trial,” conducted in 2018, was a groundbreaking study that challenged the traditional time-based approach for AIS treatment for intravenous thrombolysis. The study enrolled 503 patients who had an AIS with an unknown time of onset. Instead of relying solely on the time-based approach, the “Wake Up Trial” used advanced MRI imaging features, including the mismatch between diffusion-weighted imaging (DWI) and fluid-attenuated inversion recovery (FLAIR) in the region of ischemia, to guide thrombolysis treatment decisions. Diffusion-weighted imaging is a sensitive imaging technique that can detect early changes in brain tissue affected by ischemia, while FLAIR is a sequence that can help identify the presence of older, established infarcts.<sup>12</sup> The results of the “Wake Up Trial” showed that thrombolysis treatment guided by MRI features led to better outcomes compared to a control group that did not receive thrombolysis. Patients who received thrombolysis based on MRI findings had improved functional outcomes and higher rates of functional independence at 90 days compared to the control group.<sup>13,14</sup> Based on these findings, the most recent guidelines from the AHA recommend using MRI to evaluate the suitability of interventions in the WUS population.<sup>4</sup> However, evaluating this mismatch can be subject to significant variability when multiple readings or radiologists are involved.<sup>15</sup> Furthermore, typical MRI stroke protocols may take 10-15 minutes to perform, even with the advanced rapid protocols. Acute ischemic stroke imaging with MRI creates a mean delay of 18 minutes in workflow when compared to computed tomography (CT) scanning.<sup>16,17</sup> It is important to note that reducing the intervention time by even 15 minutes to restore blood flow can potentially lead to improved outcomes with reduced disability for a significant number of patients.<sup>18</sup> To identify relevant imaging findings in WUS patients efficiently and accurately can save time and standardize evaluation. Despite ongoing efforts to optimize stroke imaging, there is still a lack of timely and consistent stroke detection and triage methods that can be implemented immediately and in a standardized manner.

Machine learning (ML) has recently gained popularity and been used for many medical image acquisition and analysis procedures, including acquiring and reconstructing fast MR imaging data,<sup>19</sup> segmenting lesions on MR images,<sup>20</sup> classification of disease characteristics based on MRI,<sup>21</sup> and increasing the image spatial resolution.<sup>22</sup> Several studies have been reported for the use of machine learning algorithms in imaging WUS patients.<sup>23-25</sup> The main attempt of these studies is to enhance clinical outcomes by minimizing treatment delays, even if it is only by a few minutes. Machine learning algorithms are already extensively employed in patient triage for AIS treatments using computed tomography (CT).<sup>26</sup> Multiple studies have shown that automated approach based on CT is non-inferior to assessments made by experienced neuroradiologists.<sup>27-29</sup>

This systematic review aims to provide a comprehensive overview of recent advancements in utilizing ML algorithms for imaging AIS patients with MRI, with a particular emphasis on their potential implementation in clinical practice. By synthesizing current evidence and

highlighting emerging trends, this review aims to elucidate the evolving landscape of AIS imaging and the transformative role ML may play in enhancing diagnostic accuracy, prognostication, and patient management strategies. Ultimately, the integration of ML-driven MRI analysis into routine stroke care pathways has the potential to revolutionize the field, enabling more precise and personalized approaches to AIS diagnosis and treatment.

## METHODS

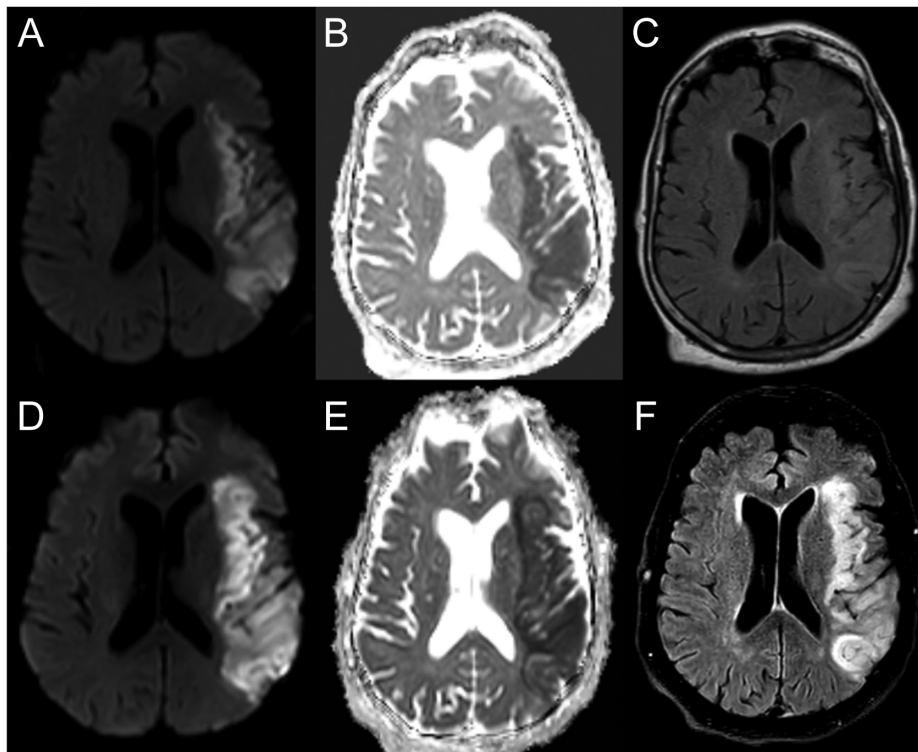
This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and conducted a search on PubMed, Web of Science, Scopus, and Google Scholar specifically targeting peer-reviewed articles in English. The predetermined search terms included “artificial intelligence,” “machine learning,” or “deep learning,” in combination with “acute ischemic stroke,” “magnetic resonance imaging,” “acute ischemic stroke onset time,” or “treatment time window.” The inclusion criteria encompassed studies that focused on predicting acute stroke onset time using magnetic resonance imaging (MRI) or identifying AIS within the therapeutic time window using MRI, and included wake-up stroke and acute stroke patients. Additionally, the studies that utilized raw MRI data as input for artificial intelligence algorithms and published after January 1, 2018, were selected. Studies involving chronic stroke patients, computed tomography, other imaging modalities, or lacking artificial intelligence were excluded from the review. Figure 1 demonstrates an AIS patient who had the progression of ischemic stroke from the acute phase (within 6 hours) to the acute–subacute stage (beyond 6 hours) in the M1 segment of the middle cerebral artery.

## RESULTS

A total of 12 papers met all inclusion and exclusion criteria. The summary of these studies is given in Table 1.

The majority of studies aimed to predict tissue at risk and the ischemic core using artificial intelligence. However, there were 2 exceptions. One study conducted by Benzakoun et al<sup>19</sup> primarily focused on the generation of synthetic data, and another conducted by Verclytte et al.<sup>30</sup> focused on accelerating image acquisition. All the mentioned studies had cohorts larger than 100 patients except the study conducted by Qun-Zhang.<sup>23</sup> Furthermore, the majority of MR images used in these studies were acquired on 1.5 T or 3T scanners.

Zhu et al<sup>31</sup> conducted a study aiming to segment the ischemic core in DWI and FLAIR images and classify lesions based on the onset time of stroke. The study utilized a multi-institutional cohort, and all images were acquired using a 3T clinical MR scanner. In this study, an automatic machine learning method was proposed to classify time since stroke (TSS) as less than or more than 4.5 hours. A cross-modal convolutional neural network (CNN) was developed to achieve accurate segmentation of stroke lesions from DWI and FLAIR images. For the segmentation tasks, 5 different EfficientNet-B0 based U-Net algorithms were employed.<sup>32</sup> Subsequently, some features were extracted from the DWI and FLAIR images based on the segmented regions of interest (ROI) using Pyradiomics.<sup>33</sup> Finally, these extracted features were provided as inputs into machine learning models to identify the TSS. Evaluation metrics such as Dice similarity coefficient, sensitivity, specificity, and accuracy were used to assess the performance of the proposed model. Remarkably, the model achieved relatively high sensitivity and specificity, both exceeding 0.80, in identifying patients who had less than 4.5 hours since the onset of a stroke.



**Figure 1.** The images demonstrate the progression of ischemic stroke from the acute phase (within 6 hours) to the acute–subacute stage (beyond 6 hours) in the M1 segment of the middle cerebral artery. A–C, acute ischemic stroke within 6 hours; D–F, acute–subacute stage of ischemic stroke beyond 6 hours. A and D, DWI with b-value of  $1000 \times 10^{-6}$  s/mm<sup>2</sup>; B and E, ADC map; C and F, FLAIR image.

In addition, Ho and colleagues conducted studies in 2018<sup>34</sup> and 2019<sup>24</sup> focusing on determining stroke time onset utilizing MRI through the application of deep learning, with a specific emphasis on autoencoders. Although these studies were innovative, they had the drawback of utilizing only their institutional cohort for analysis. The studies utilized MRI images acquired on 1.5 and 3 T clinical scanners. The imaging modalities included DWI, Apparent Diffusion Coefficient (ADC), Perfusion-Weighted Imaging (PWI), and FLAIR. Perfusion-weighted imaging images were used to generate perfusion parameters such as mean transit time (MTT), time to peak (TTP), cerebral blood volume (CBV), cerebral blood flow (CBF), and time to maximum (Tmax). A threshold of Tmax > 6 seconds was employed for segmentation of the ROIs. In the 2018 study, baseline features were extracted by determining the mean intensity values of the images at ROIs. Deep learning algorithms based on autoencoders were then used to extract hidden PWI features. Both baseline and hidden features were utilized to devise machine learning algorithms. The classification task, aimed at identifying a TSS of less than 4.5 hours using only baseline features, achieved an area under the curve (AUC) of 0.57. However, the inclusion of both baseline and deep features enhanced the classification task, elevating the AUC to 0.68.<sup>34</sup> In a subsequent study in 2019, the same group enriched the extraction of baseline features by incorporating additional descriptive features, namely mean, median, skewness, and kurtosis, while maintaining the deep learning aspect of the study intact. The combination of autoencoder-based deep features and baseline features achieved the best performance in predicting TSS of less than 4.5 hours, with an AUC of 0.76.<sup>24</sup>

In 2020, Yu et al<sup>35</sup> embarked on a study aimed at predicting the final ischemic core, an area of permanent tissue damage following a stroke, using baseline MRI and deep learning techniques. This study

brought together 182 patients from 2 separate cohorts across different institutions. The patients underwent clinical MR scans at 1.5 T and 3 T, employing various imaging modalities, including DWI, PWI, T2-weighted MRI (T2W), and FLAIR. The team used PWI to obtain perfusion parameter maps and established tissue-at-risk parameters based on a Tmax exceeding 6 seconds, while identifying the ischemic core with an ADC below  $620 \times 10^{-6}$  mm<sup>2</sup>/s. The “ground truth” data, or verified data used for comparison with predictions, was sourced from T2W-MRI and FLAIR scans taken 3–7 days post stroke. A deep learning model utilizing an attention-gated U-Net, which incorporated consecutive slices of various imaging data and masks of Tmax and ADC, achieved a median AUC of 0.92 in identifying the final infarction without accounting for any subsequent reperfusion in the patients. Similarly, in 2021, the same researchers aimed to estimate tissue at risk and the ischemic core using the same deep learning approach.<sup>36</sup> This study exhibited superiority compared to the former study in terms of including more patients from 3 prospective multicenter stroke trials. The MR images were acquired at 1.5 T and 3 T MRI scanners, employing the same imaging modalities as the previous study. An attention-gated U-Net, with an identical architecture to the aforementioned study, was utilized. It incorporated 5 consecutive slices of DWI, ADC, Tmax, MTT, CBF, and CBV images, along with masks of Tmax and ADC, as inputs. The key difference between these 2 studies centered on considering the patient’s reperfusion status during the training phase. This status was categorized into minimal (20%), partial (20%–80%), and major (80%) reperfusion, determined based on a 4–24-hour follow-up PWI. The segmentation task utilizing the attention-gated U-Net outperformed the thresholding method that relied on DWI/PWI thresholds. The proposed deep learning method achieved an AUC of 0.97 for predicting the ischemic core.

**Table 1.** Summary of MRI of Ischemic Stroke Studies Utilizing Artificial Intelligence

Study	Number of Patients	MRI		MRI Sequences	AI Methods	Conclusion
		Scanner Field Strength	AI Tasks			
Zhu et al <sup>31</sup>	268	3 T	Segmentation and classification	FLAIR and DWI	Deep CNN (U-Net) for segmentation, feature extraction by Pyradiomics, and ML for classification	Segmentation task dice score for FLAIR <0.80, dice score for DWI >0.80, classification task with ML using features extracted from manual labeling and segmentation ROI are around 0.80.
Chung Ho et al <sup>24</sup>	181	1.5 and 3 T	Classification	PWI, FLAIR, DWI, and ADC	Deep feature maps were extracted from PWI by deep autoencoder. ML classification was used for morphological and descriptive features including mean, median, etc. The total number of baseline features = 104, deep features = 384	Classification task with ML achieved an AUC of 0.76 using perfusion parameters map + deep features
Chung Ho et al <sup>34</sup>	105	1.5 and 3 T	Classification	PWI, DWI, FLAIR and ADC	Deep feature maps were extracted from PWI by deep autoencoder. ML classification was used for the intensity value of perfusion parameter maps, DWI, FLAIR and ADC. The total number of baseline features = 7	Classification tasks with ML achieved an AUC of 0.57 using baseline features. The classification task with ML achieved an AUC of 0.68 using baseline and deep features
Yu et al <sup>36</sup>	237	1.5 and 3 T	Segmentation	DWI, ADC, Tmax, MTT, CBV, CBF	Attention-gated U-Net was used for segmentation tasks. Tmax > 6 seconds was used to define tissue at risk and ADC < 620 × 10 <sup>-6</sup> mm <sup>2</sup> /s for ischemic core. T2 and FLAIR acquired at 3-7 days were used as ground truth.	Segmentation task with attention-gated U-Net outperformed thresholding method which uses DWI/PWI thresholds. The proposed deep learning method achieves 0.97 AUC to predict ischemic core.
Do et al. <sup>37</sup>	390	1.5 T	Classification	DWI	ASPECT score prediction with recurrent residual convolutional neural network	Proposed model RRCNN outperformed the pre-trained CNN with accuracy of 87.3
Nazari-Farsani et al <sup>38</sup>	445	1.5 and 3 T	Segmentation	DWI, ADC, and thresholded ADC as input and T2-FLAIR and DWI for ground truth	Attention gated U-Net is used for delineation ischemic core.	The DCNN model predicted the final stroke lesions significantly better than the simple ADC thresholding method with AUC of 0.91 with dice similarity coefficient threshold of 0.50
Benzakoun et al <sup>19</sup>	1416	1.5 T	Synthetic data generation	DWI and FLAIR	Generative adversarial network was used for generation of synthetic FLAIR from DWI images.	Synthetic FLAIR had diagnostic performances similar to real FLAIR in depicting DWI-FLAIR mismatch
Vercllyte et al <sup>30</sup>	173	3 T	MR reconstruction	T2W, T2W*, FLAIR, and DWI	Deep learning methods were used for acceleration of acquisition	The study highlights the high performance and reproducibility of the ultrafast MRI protocol in the acute ischemic stroke assessment
Wang et al <sup>39</sup>	137	1.5 and 3 T	Segmentation	pCASL, ADC, and Tmax	High-resolution 3Dnet were trained by ASL, Tmax, and ADC. PWI images were used for ground truth.	The study trained DL models with an input of noncontrast ASL images, using the hypoperfusion lesion observed on DSC MRI as the label. The model achieved an accuracy of 0.92 for image-based decision.
Yu et al <sup>35</sup>	182	1.5 and 3 Te	Segmentation	DWI, ADC, Tmax, MTT, CBV, CBF	Attention-gated U-Net was used for segmentation tasks. Tmax > 6 sec was used to define tissue at risk and ADC < 620 × 10 <sup>-6</sup> mm <sup>2</sup> /s for ischemic core. T2WI and FLAIR acquired at 3-7 days were used as ground truth.	Segmentation task with attention-gated U-Net outperformed thresholding method which uses DWI/PWI thresholds. Deep learning methods achieved moderate to excellent segmentation tasks for both ischemic core and tissue at risk.
Zhang et al <sup>25</sup>	422	1.5 and 3 T	Classification	T2W, DWI, and FLAIR	Attention-gated pre-trained weights were used for feature extraction and classification in a single slice. Attention-gated 3D U-Net and CNN from scratch was used for feature extraction and classification.	The pretrained 2D model achieved the highest performance metrics with a sensitivity of 0.70 and a specificity of 0.81 in classifying TSS < 4.5 hours.
Zhang et al <sup>23</sup>	84	3 T	Classification	ADC, DWI, and T1W	Radiomics features were used for feature extraction. ML and DL were used for classification.	DL model achieved the highest performance with an accuracy of 0.72 than conventional ML methods.

Furthermore, Do et al<sup>37</sup> conducted a study with the aim of classifying DWI images based on Alberta Stroke Program Early CT Score (ASPECTS) using deep learning algorithms. The study included 390 DWI scans acquired on a 1.5 T MRI scanner. The researchers developed a classifier algorithm to differentiate between low (1-6) and high (7-10) DWI-ASPECTS groups. Two different deep learning algorithms were compared in the study, a recurrent residual convolutional neural network (RRCNN) and a pre-trained 3D CNN, as well as a 3D CNN trained from scratch. The performance of these algorithms was evaluated and compared. The researchers concluded that the proposed model based on RRCNN outperformed both the pre-trained 3D CNN and the 3D CNN trained from scratch. The RRCNN achieved an accuracy of 0.87 in the classification task, demonstrating its superior performance in distinguishing between low and high DWI-ASPECTS groups.

Additionally, Nazari-Farsani et al<sup>38</sup> conducted a study aiming to predict the final ischemic core from baseline DWI data using deep learning. The strength of this study lies in its patient cohort, which consisted of 445 patients recruited from multiple institutions. The ground truth for the final ischemic core was determined using T2W and FLAIR scans taken 3-7 days after stroke onset. For the segmentation tasks, an attention-gated U-Net was employed. The inputs to the model included DWI, ADC, and thresholded regions with ADC values of less than  $620 \times 10^{-6} \text{ mm}^2/\text{s}$ . The model generated a voxel-by-voxel probability map of tissue infarction as the output. A deep convolutional neural network (CNN) model outperformed the simple ADC thresholding method in predicting the final stroke lesions. It achieved an AUC of 0.91 with a dice similarity coefficient threshold of 0.50, demonstrating its superior performance and accuracy in segmenting the ischemic core.

Moreover, Benzakoun et al<sup>19</sup> conducted a study with the objective of generating synthetic FLAIR images from DWI to assess the DWI-FLAIR mismatch sign as a surrogate for identifying patients who experienced acute ischemic stroke within 4.5 hours of onset. The study included a substantial cohort of 1416 patients. The deep learning model employed in this study was developed based on an edge-aware generative adversarial network (GAN). It was trained on a dataset consisting of DWI, ADC map, and FLAIR images. After completing the training process, synthetic FLAIR images were generated for the test set using the DWI and ADC images. The study's findings demonstrated that by eliminating the need for real FLAIR images in the MRI protocol and instead generating FLAIR images during the acquisition of other sequences, a significant time-saving of approximately 25% can be achieved during scanning. This approach offered a promising strategy for improving efficiency in acute ischemic stroke imaging protocols.

In another work, Verclytte et al<sup>30</sup> conducted a study with the objective of accelerating the acquisition of MRI protocols using deep learning reconstruction techniques. The study involved 173 patients who underwent MRI scans with a 3T scanner in a prospective design. Each patient's MRI protocol consisted of reference acquisitions of T2-FLAIR, DWI, and SWI, which had a total duration of 7 minutes and 54 seconds. Additionally, accelerated multi-shot EPI counterparts for T2-FLAIR and T2\* were obtained, along with a single-shot EPI DWI scan, which had a shorter duration of 1 minute and 54 seconds. To achieve accelerated MRI acquisition, the researchers employed an ultra-fast approach using multiple echo planar imaging (EPI). Furthermore, a new deep learning reconstruction technique was integrated to enhance the signal-to-noise ratio (SNR) of the acquired images. By leveraging this ultra-fast MRI protocol, which included multi-shot EPI counterparts for T2, T2\*, and T2-FLAIR, as well as fast single-shot EPI-based

DWI, the duration of the MRI protocol was reduced by 6 minutes. Importantly, the study found that the differential diagnoses obtained using the accelerated MRI protocol were similar to those obtained with the reference acquisitions.

Besides, Wang et al<sup>39</sup> conducted a study with the objective of delineating the ischemic core and tissue at risk in 3-dimensional (3D) pseudo continuous Arterial Spin Labeling (pCASL) images and DWI, using PWI as the ground truth. The study included a total of 137 patients with acute ischemic stroke, and images were acquired using 1.5 T and 3 T clinical MRI scanners. The hypoperfusion area was identified using  $T_{\text{max}} > 6$  seconds as the ground truth. The researchers employed Highres3DNet,<sup>40</sup> a deep learning algorithm that was trained using CBF and ADC images as well as the label of  $T_{\text{max}}$ . The eligibility for endovascular treatment was retrospectively determined based on the criteria of perfusion/diffusion mismatch in the DEFUSE 3 trial.<sup>9</sup> Subsequently, the trained deep learning algorithm was applied to 12 3D pCASL datasets without fine-tuning of parameters. The algorithm demonstrated the ability to predict the hypoperfusion region defined by dynamic susceptibility contrast in pCASL, achieving a voxel-wise AUC of 0.958.

On top of that, Zhang et al<sup>25</sup> conducted a study with the aim of predicting the onset time of acute ischemic stroke. The study included a total of 422 patients who underwent MRI scans using 1.5 T and 3 T clinical MRI scanners. The inputs for the deep learning architecture consisted of DWI, FLAIR, and T2W MRI. The proposed approach utilized a transfer learning method within the same domain, focusing on adapting the model for an intra-domain task. Initially, the model was trained on a relatively simpler clinical task, specifically stroke detection. This initial training served as a foundation for the subsequent fine-tuning and refinement of the model using various binary thresholds of TSS, aiming to improve its performance and adaptability. The proposed approach was tested using both 2D and 3D deep learning architectures, including an attention-gated pre-trained 2D CNN, 3D U-Net, and 3D CNN trained from scratch. Among these models, the pre-trained 2D CNN achieved the highest performance metrics with a sensitivity of 0.70 and a specificity of 0.81 in classifying TSS of less than 4.5 hours.

Lastly, Qun Zhang et al<sup>23</sup> conducted a study with the objective of predicting the onset time of acute stroke within the intervention window. The study involved 84 patients who underwent MRI scans using a 3 T clinical MRI scanner. Baseline images including ADC, DWI, and T1W MRI were acquired for each patient. To extract relevant information, ROIs were manually segmented on the DWI images. Radiomics features were then extracted from the ADC, DWI, and T1W MRI images based on the segmented ROIs, following image registration. Various preprocessing techniques and feature selection methods were applied to refine the data. Both conventional machine learning algorithms and deep learning algorithms were employed for the classification task. The machine learning algorithms utilized the selected features to predict the onset time of acute stroke, while the deep learning algorithm leveraged the power of neural networks for the same task. Notably, the DL model achieved the highest performance among the different methods tested, achieving an accuracy of 0.72.

## DISCUSSION

The studies included in this review covered different aspects of MR imaging of acute ischemic stroke utilizing machine learning algorithms. The primary objectives of most studies were to predict tissue at risk, identify the ischemic core, and classify patients who experienced

acute ischemic stroke within the treatment window. However, 2 studies had alternative goals, which focused on generating synthetic data<sup>19</sup> and accelerating MR image acquisition.<sup>30</sup>

The extensive utilization of machine learning algorithms in segmentation tasks is of utmost importance in accurately detecting the infarct core from cross-sectional imaging. This is particularly significant as the determination of the infarct core plays a vital role in assessing eligibility for revascularization procedures in treatment.<sup>41</sup> Additionally, given the time-sensitive nature of acute ischemic stroke treatment, it is not surprising that one of the major applications of machine learning has been the identification of patients within the appropriate treatment time window. Various deep learning techniques were employed in these studies, including CNNs, U-Net, autoencoders, and GANs, demonstrating their potentials in segmenting the ischemic core, classifying lesions based on onset time, predicting tissue at risk, and expediting the MRI protocol. The majority of MRI protocols used in these studies primarily included ADC, DWI, FLAIR, and T2W images. The integration of advanced imaging techniques such as PWI and pCASL further improved the accuracy of the deep learning models. However, it is necessary to take into account the increase in total scan time, since a delay of 10 minutes in treatment was reported to cost approximately \$249 million annually in a recent health economics study.<sup>42</sup> Furthermore, the utilization of attention-gated and pretrained networks enhanced the model performances. An attention-gated network selectively focuses on relevant features or regions of an input using an attention mechanism, while a pretrained network refers to a model that has been previously trained on a related task or a large dataset, providing a starting point and improving subsequent model performance. Only 1 study, which was conducted by Zhang et al.,<sup>25</sup> employed intra-domain task adaptive transfer learning to enhance the performance of the model, where the model was initially trained on stroke detection to enhance its performance. The use of machine learning algorithms with deep features has also been reported to enhance accuracy.<sup>34</sup>

## CONCLUSION

The objective of our research is to provide an overview of the latest developments in the utilization of ML algorithms for MRI-based imaging of patients with AIS. The main focus is on how these advancements could potentially be applied in real-world clinical settings. To accomplish this goal, the PRISMA guidelines were followed, and clear inclusion and exclusion criteria were established. A total of 12 relevant papers were identified and included.

To the best of our knowledge, the significance of this study lies in the provision of a novel literature review regarding the utilization of MRI-based machine learning in patients with AIS. Typically, AIS imaging relies on CT scans in the emergency room, with limited use of MRI in this context. Through this review, it is emphasized that MRI, aided by machine learning, may potentially be employed as effectively as CT in the diagnosis and assessment of AIS. The application of AI in MRI of stroke has demonstrated significant progress in tasks such as image segmentation, classification, and prediction. These advancements offer the potential to improve the accuracy and efficiency of stroke diagnosis and treatment planning. However, it is crucial to acknowledge that there is a range of algorithm performances. These variations may be attributed to the use of different accuracy measures, the evaluation of various systems against diverse standards, and the utilization of input data with varying qualities. Such disparities can result in inconsistent and potentially biased differences in study conclusions. To ensure the

robustness of these findings, it is imperative to further validate and generalize the results of AI studies in stroke by including larger and more diverse patient cohorts. In the future, we anticipate witnessing an increased number of ML techniques applied in MRI, particularly with a focus on acute ischemic stroke.

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## REFERENCES

- Ovbiagele B, Nguyen-Huynh MN. Stroke epidemiology: advancing our understanding of disease mechanism and therapy. *Neurotherapeutics*. 2011;8(3):319-329. [\[CrossRef\]](#)
- Soun JE, Chow DS, Nagamine M, et al. Artificial intelligence and acute stroke imaging. *AJNR Am J Neuroradiol*. 2021;42(1):2-11. [\[CrossRef\]](#)
- Boursin P, Paternotte S, Dercy B, Sabben C, Maier B. Semantics, epidemiology and semiology of stroke. *Soins*. 2018;63(828):24-27. [\[CrossRef\]](#)
- Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019;50(12):e344-e418. [\[CrossRef\]](#)
- Albers GW, Lansberg MG, Kemp S, et al. A multicenter randomized controlled trial of endovascular therapy following imaging evaluation for ischemic stroke (DEFUSE 3). *Int J Stroke*. 2017;12(8):896-905. [\[CrossRef\]](#)
- Tsivgoulis G, Katsanos AH, Sandset EC, et al. Thrombolysis for acute ischaemic stroke: current status and future perspectives. *Lancet Neurol*. 2023;22(5):418-429. [\[CrossRef\]](#)
- Saver JL. Time is brain—quantified. *Stroke*. 2006;37(1):263-266. [\[CrossRef\]](#)
- Liebeskind DS, Saber H, Xiang B, et al. Collateral circulation in thrombectomy for stroke after 6 to 24 hours in the DAWN trial. *Stroke*. 2022;53(3):742-748. [\[CrossRef\]](#)
- Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378(8):708-718. [\[CrossRef\]](#)
- Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2018;378(1):11-21. [\[CrossRef\]](#)
- Elfil M, Eldokmak M, Baratloo A, Ahmed N, Amin HP, Koo BB. Pathophysiological mechanisms, neuroimaging and treatment in wake-up stroke. *CNS Spectr*. 2020;25(4):460-467. [\[CrossRef\]](#)
- Srinivasan A, Goyal M, Al Azri F, Lum C. State-of-the-art imaging of acute stroke. *RadioGraphics*. 2006;26(suppl 1):S75-S95. [\[CrossRef\]](#)
- Rimmele DL, Thomalla G. Wake-up stroke: clinical characteristics, imaging findings, and treatment option - an update. *Front Neurol*. 2014;5:35. [\[CrossRef\]](#)
- Thomalla G, Simonsen CZ, Boutitie F, et al. MRI-guided thrombolysis for stroke with unknown time of onset. *N Engl J Med*. 2018;379(7):611-622. [\[CrossRef\]](#)
- Thomalla G, Cheng B, Ebinger M, et al. DWI-FLAIR mismatch for the identification of patients with acute ischaemic stroke within 4-5 h of symptom onset (PRE-FLAIR): a multicentre observational study. *Lancet Neurol*. 2011;10(11):978-986. [\[CrossRef\]](#)
- Menon BK, Almekhlafi MA, Pereira VM, et al. Optimal workflow and process-based performance measures for endovascular therapy in acute ischemic stroke: analysis of the solitaire FR thrombectomy for acute revascularization study. *Stroke*. 2014;45(7):2024-2029. [\[CrossRef\]](#)
- Nael K, Khan R, Choudhary G, et al. Six-minute magnetic resonance imaging protocol for evaluation of acute ischemic stroke: pushing the boundaries. *Stroke*. 2014;45(7):1985-1991. [\[CrossRef\]](#)

18. Sheth SA, Jahan R, Gralla J, et al. Time to endovascular reperfusion and degree of disability in acute stroke. *Ann Neurol*. 2015;78(4):584-593. [\[CrossRef\]](#)
19. Benzakoun J, Deslys MA, Legrand L, et al. Synthetic FLAIR as a substitute for FLAIR sequence in acute ischemic stroke. *Radiology*. 2022;303(1):153-159. [\[CrossRef\]](#)
20. Liu CF, Hsu J, Xu X, et al. Deep learning-based detection and segmentation of diffusion abnormalities in acute ischemic stroke. *Commun Med (Lond)*. 2021;1:61. [\[CrossRef\]](#)
21. Jiang L, Zhang C, Wang S, et al. MRI Radiomics features from infarction and cerebrospinal fluid for prediction of cerebral edema after acute ischemic stroke. *Front Aging Neurosci*. 2022;14:782036. [\[CrossRef\]](#)
22. Li BM, Castorina LV, Valdés Hernández MDC, et al. Deep attention super-resolution of brain magnetic resonance images acquired under clinical protocols. *Front Comput Neurosci*. 2022;16:887633. [\[CrossRef\]](#)
23. Zhang YQ, Liu AF, Man FY, et al. MRI radiomic features-based machine learning approach to classify ischemic stroke onset time. *J Neurol*. 2022;269(1):350-360. [\[CrossRef\]](#)
24. Ho KC, Speier W, Zhang H, Scalzo F, El-Saden S, Arnold CW. A machine learning approach for classifying ischemic stroke onset time from imaging. *IEEE Trans Med Imaging*. 2019;38(7):1666-1676. [\[CrossRef\]](#)
25. Zhang H, Polson JS, Nael K, et al. Intra-domain task-adaptive transfer learning to determine acute ischemic stroke onset time. *Comput Med Imaging Graph*. 2021;90:101926. [\[CrossRef\]](#)
26. Jiang F, Jiang Y, Zhi H, et al. Artificial intelligence in healthcare: past, present and future. *Stroke Vasc Neurol*. 2017;2(4):230-243. [\[CrossRef\]](#)
27. Nagel S, Sinha D, Day D, et al. e-ASPECTS software is non-inferior to neuroradiologists in applying the ASPECT score to computed tomography scans of acute ischemic stroke patients. *Int J Stroke*. 2017;12(6):615-622. [\[CrossRef\]](#)
28. Herweh C, Ringleb PA, Rauch G, et al. Performance of e-ASPECTS software in comparison to that of stroke physicians on assessing CT scans of acute ischemic stroke patients. *Int J Stroke*. 2016;11(4):438-445. [\[CrossRef\]](#)
29. Guberina N, Dietrich U, Radbruch A, et al. Detection of early infarction signs with machine learning-based diagnosis by means of the Alberta Stroke Program Early CT score (ASPECTS) in the clinical routine. *Neuroradiology*. 2018;60(9):889-901. [\[CrossRef\]](#)
30. Vercllytte S, Gnanih R, Verdun S, et al. Ultrafast MRI using deep learning echo planar imaging for a comprehensive assessment of acute ischemic stroke. *Eur Radiol*. 2023;33(5):3715-3725. [\[CrossRef\]](#)
31. Zhu H, Jiang L, Zhang H, Luo L, Chen Y, Chen Y. An automatic machine learning approach for ischemic stroke onset time identification based on DWI and FLAIR imaging. *NeuroImage Clin*. 2021;31:102744. [\[CrossRef\]](#)
32. Tan M, Le Q. *Efficient Net: rethinking model scaling for convolutional neural networks*. International conference on machine learning [\[CrossRef\]](#) 2019. <http://proceedings.mlr.press/v97/tan19a.html?ref=jina-ai-gmbh.ghost.io>
33. van Griethuysen JJM, Fedorov A, Parmar C, et al. Computational Radiomics system to decode the radiographic phenotype. *Cancer Res*. 2017;77(21):e104-e107. [\[CrossRef\]](#)
34. Ho KC, Speier W, El-Saden S, Arnold CW. Classifying acute ischemic stroke onset time using deep imaging features. *AMIA Annu Symp Proc*. 2017;2017:892-901. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5977679>
35. Yu Y, Xie Y, Thamm T, et al. Use of deep learning to predict final ischemic stroke lesions from initial magnetic resonance imaging. *JAMA Netw Open*. 2020;3(3):e200772. [\[CrossRef\]](#)
36. Yu Y, Xie Y, Thamm T, et al. Tissue at risk and ischemic core estimation using deep learning in acute stroke. *AJNR Am J Neuroradiol*. 2021;42(6):1030-1037. [\[CrossRef\]](#)
37. Do LN, Baek BH, Kim SK, Yang HJ, Park I, Yoon W. Automatic assessment of ASPECTS using diffusion-weighted imaging in acute ischemic stroke using recurrent residual convolutional neural network. *Diagnostics (Basel)*. 2020;10(10). [\[CrossRef\]](#)
38. Nazari-Farsani S, Yu Y, Duarte Armindo R, et al. Predicting final ischemic stroke lesions from initial diffusion-weighted images using a deep neural network. *NeuroImage Clin*. 2023;37:103278. [\[CrossRef\]](#)
39. Wang K, Shou Q, Ma SJ, et al. Deep learning detection of penumbral tissue on arterial spin labeling in stroke. *Stroke*. 2020;51(2):489-497. [\[CrossRef\]](#)
40. Niethammer M, Styner M, Aylward S, et al. Information Processing in Medical Imaging: 25th International Conference, IPMI 2017, Boone, NC, USA, June 25-30, 2017, Proceedings [\[CrossRef\]](#) Springer; 2017. <https://play.google.com/store/books/details?id=r8gmDwAAQBAJ>
41. Catanese L, Tarsia J, Fisher M. Acute ischemic stroke therapy overview. *Circ Res*. 2017;120(3):541-558. [\[CrossRef\]](#)
42. Kunz WG, Hunink MG, Almekhlafi MA, et al. Public health and cost consequences of time delays to thrombectomy for acute ischemic stroke. *Neurology*. 2020;95(18):e2465-e2475. [\[CrossRef\]](#)