ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 9, Issue – 1, February - 2026, Page No.: 120 – 129

Quantitative Attenuation-Based Temporal Staging of Ischemic Cerebral Infarction on CT with MRI Correlation

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How to citation this article: Dr. Suhas C. M., Dr. Vinay M. D. Prabhu, "Quantitative Attenuation-Based Temporal Staging of Ischemic Cerebral Infarction on CT with MRI Correlation", IJMACR- February - 2026, Volume – 9, Issue - 1, P. No. 120 – 129.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Accurate temporal staging of ischemic cerebral infarction is essential for appropriate therapeutic decision-making and characterisation in acute stroke management. Non-contrast computed tomography (CT) remains the first-line imaging modality due to its rapid acquisition and widespread availability. However, staging is frequently based on subjective visual interpretation. Quantitative assessment using Hounsfield Unit (HU) attenuation values may provide an objective method for differentiating infarct stages. Given the increasing emphasis on quantitative imaging biomarkers in neuroradiology, objective attenuation-based stratification may reduce observer dependency and enhance reproducibility in routine stroke assessment.

Aims and Objectives:

To evaluate the role of quantitative CT attenuation values in categorizing ischemic cerebral infarction into acute, subacute, and chronic stages with clinical correlation, and to derive stage-specific reference HU ranges for prospective CT-based categorization.

Methodology: A retrospective study was conducted on 254 patients diagnosed with ischemic cerebral infarction who underwent non-contrast CT over an 18-month period in a tertiary care hospital. Infarcts were classified into acute (6–48 hours), subacute (48 hours–14 days), and chronic (>14 days) stages based on clinical history and duration of symptoms. Three standardized regions of interest were placed within the infarcted parenchyma, and the mean attenuation value was calculated for analysis. Intergroup comparison was performed using appropriate statistical tests. Interobserver agreement was

assessed in 30 randomly selected cases using intraclass correlation coefficient. A subset of 32 patients who also underwent subsequent magnetic resonance imaging was included for validation, and CT-based temporal staging was compared with MRI features of infarct evolution to assess concordance.

Results: Among 254 cases, 71 (28%) were acute, 102 (40%) subacute, and 81 (32%) chronic infarcts. The mean attenuation values of the ischemic region were 25.98 HU in acute, 18.76 HU in subacute, and 11.16 HU in chronic infarcts. The mean attenuation values were 25.98 ± 2.8 HU in acute, 18.76 ± 3.9 HU in subacute, and 11.16 ± 2.2 HU in chronic infarcts. Percentile-based distribution analysis demonstrated stage-specific attenuation intervals: acute infarcts (23.7–31 HU), subacute infarcts (14.5–24.5 HU), and chronic infarcts (8.3–14 HU). These attenuation distributions showed statistically significant differences among the three stages ($p < 0.001$). The derived percentile-based intervals provided clear separation across stages, supporting objective temporal stratification. Interobserver reliability was excellent, with an intraclass correlation coefficient of 0.91. In the MRI validation subset, CT-based staging demonstrated concordance with MRI findings in 29 of 32 cases (90.6%).

Conclusion:

Quantitative Hounsfield Unit analysis on non-contrast CT provides an objective and reproducible method for temporal staging of ischemic cerebral infarction. The percentile-derived attenuation intervals demonstrated clear stage-wise separation and may serve as cohort-based reference standards for prospective CT-based categorization. This quantitative approach enhances diagnostic confidence in acute stroke evaluation and offers a practical imaging biomarker framework, particularly in settings where advanced imaging modalities are unavailable or contraindicated. The high concordance observed in the MRI validation subset further reinforces the biological reliability of attenuation-based temporal stratification and supports its potential application in routine clinical practice.

Keywords: Ischemic cerebral infarction, non-contrast computed tomography, Hounsfield Unit, CT attenuation values, temporal staging, stroke imaging.

Introduction

Ischemic cerebral infarction represents a major cause of morbidity and mortality worldwide and accounts for the majority of cerebrovascular accidents[1,2]. Rapid and accurate assessment of infarct timing is critical in acute stroke management, as therapeutic decisions such as thrombolysis and endovascular intervention are highly time-dependent[3]. Early imaging evaluation therefore plays a central role in patient triage and clinical decision-making.

Non-contrast computed tomography (CT) remains the first-line imaging modality in acute stroke settings because of its rapid acquisition, widespread availability, and ability to reliably exclude intracranial hemorrhage[3,4]. Although CT is sensitive for established infarction, early ischemic changes may be subtle and are frequently interpreted qualitatively based on parenchymal hypodensity, sulcal effacement, and loss of gray–white matter differentiation[5]. Such subjective interpretation may demonstrate interobserver variability and can be influenced by observer experience[6].

Hounsfield Units (HU) provide a standardized quantitative scale for measuring tissue attenuation on CT imaging[7]. Alterations in attenuation during the evolution of ischemic infarction reflect underlying pathophysiological mechanisms including cytotoxic

edema in the acute stage, progression to vasogenic edema in the subacute phase, and eventual gliotic transformation in the chronic stage[8]. Progressive reduction in CT attenuation values across stages of infarction suggests that quantitative assessment may provide an objective method for temporal differentiation. Progressive reduction in attenuation values has been documented across stages of infarction; however, systematic derivation of stage-specific attenuation intervals remains limited in literature

Quantitative imaging approaches are increasingly recognized as valuable tools in modern radiology, enabling objective assessment, improved reproducibility, and reduction of observer-dependent variability[9]. Establishing stage-wise attenuation reference intervals for ischemic infarction may enhance diagnostic confidence and provide a practical framework for CT-based temporal stratification, particularly in settings where advanced imaging modalities such as magnetic resonance imaging are unavailable or contraindicated.

The present study aims to evaluate quantitative CT attenuation values in categorizing ischemic cerebral infarction into acute, subacute, and chronic stages with clinical correlation, and to derive percentile-based attenuation reference intervals that may serve as cohort-derived standards for prospective CT-based temporal classification.

While CT remains the primary modality in acute stroke evaluation, validation of CT-based temporal classification against magnetic resonance imaging findings may enhance confidence in attenuation-derived staging. MRI sequences such as diffusion-weighted imaging, apparent diffusion coefficient maps and fluid-attenuated inversion recovery provide well-established markers of infarct evolution and can serve as biological correlates for temporal assessment. Integrating MRI correlation may therefore strengthen the reliability of quantitative CT-based stratification.

Materials and Methods

Study Design and Duration: A retrospective observational study was conducted over an 18-month period in the Department of Radio-Diagnosis at a tertiary care teaching hospital.

Study Population: A total of 254 patients diagnosed with ischemic cerebral infarction on non-contrast computed tomography were included in the study.

Inclusion Criteria

- Patients aged ≥18 years
- CT brain demonstrating ischemic cerebral infarction
- Documented clinical history with clearly defined time of symptom onset.

Exclusion Criteria

- Hyper acute infarction
- Hemorrhagic transformation
- Mixed ischemic–hemorrhagic lesions
- Post-surgical changes
- Space-occupying lesions mimicking infarct
- Poor image quality or motion artifacts

Temporal Classification

Based on clinical presentation and duration from symptom onset to imaging, infarcts were categorized into:

Acute: 6–48 hours

Subacute: 48 hours–14 days

Chronic: >14 days

CT Acquisition Protocol

All patients underwent non-contrast CT brain using a multi-detector CT scanner. Imaging parameters included standard brain protocol with axial sections and later reconstructed at 1 mm slice thickness.

Attenuation Measurement Technique

Attenuation measurements were performed on axial sections showing maximum infarct extent. Three standardized circular regions of interest were placed within the infarcted parenchyma, carefully avoiding:

Adjacent cerebrospinal fluid spaces

Hemorrhagic components

Calcifications

Beam-hardening artifacts

The mean of the three Hounsfield Unit measurements was recorded for statistical analysis.

Interobserver Agreement

To assess reproducibility, a second radiologist independently measured attenuation values in 30 randomly selected cases, blinded to clinical staging and initial readings. Interobserver reliability was calculated using the intraclass correlation coefficient.

MRI correlation in subset

A subset of 32 patients underwent magnetic resonance imaging within a short interval following CT examination. MRI studies included diffusion-weighted imaging, apparent diffusion coefficient maps, and fluid-attenuated inversion recovery sequences. CT-based temporal classification was compared with MRI features consistent with acute (diffusion restriction), subacute (FLAIR evolution with variable diffusion characteristics), and chronic (encephalomalacia and gliosis) infarction. Concordance between CT-based staging and MRI findings was assessed descriptively.

Statistical Analysis

Statistical analysis was performed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation. Normality of attenuation data was assessed using the Shapiro–Wilk test. One-way analysis of variance was performed for intergroup comparison, followed by Tukey post-hoc testing for pairwise differentiation. Receiver operating characteristic analysis was conducted using individual patient-level attenuation values to determine stage-wise discriminatory performance.

Receiver Operating Characteristic Analysis

Receiver operating characteristic (ROC) analysis was performed using individual patient-level attenuation values to evaluate the discriminative performance of CT attenuation in differentiating infarct stages. The area under the curve (AUC) was calculated for adjacent stage comparisons, and optimal threshold values were determined based on ROC curve analysis.

Results

Demographic Profile: A total of 254 patients with ischemic cerebral infarction were included in the study. The mean age of the study population was 65.6 years, with a percentile distribution ranging from 54 to 77.2 years. Of the total cases, 188 (74%) were males and 66 (26%) were females, demonstrating a male predominance.

Stage Distribution

Based on clinical duration from symptom onset to imaging, infarcts were categorized into acute, subacute, and chronic stages. Among the study population, 71 (28%) were acute, 102 (40%) were subacute, and 81 (32%) were chronic infarcts.

Attenuation Values Across Stages

Quantitative attenuation analysis demonstrated a progressive reduction in mean Hounsfield Unit values corresponding to infarct evolution. The mean attenuation values were 25.98 ± 2.8 HU in acute, 18.76 ± 3.9 HU in subacute, and 11.16 ± 2.2 HU in chronic infarcts. One-way analysis of variance demonstrated statistically significant differences among groups ($p < 0.001$). Post-

hoc pairwise comparison confirmed significant differentiation between each stage.

Percentile-Based Attenuation Intervals

Percentile distribution analysis (10th–90th percentile) was performed to derive stage-specific attenuation intervals. The derived attenuation ranges were:

Acute infarcts: 23.7–31 HU

Subacute infarcts: 14.5–24.5 HU

Chronic infarcts: 8.3–14 HU

Although minimal overlap was observed at percentile margins between adjacent stages, overall attenuation distributions demonstrated clear stage-wise differentiation.

Interobserver Agreement

Interobserver reliability was assessed in 30 randomly selected CT studies. Attenuation measurements demonstrated excellent agreement between observers, with an intraclass correlation coefficient of 0.91, indicating high reproducibility of the standardized measurement protocol.

MRI Correlation

Among the 32 patients who underwent subsequent magnetic resonance imaging within a short interval following CT examination, CT-based temporal staging demonstrated concordance with MRI features of infarct evolution in 29 cases (90.6%). The three discordant cases were observed near clinical stage transition intervals, suggesting biological overlap during infarct evolution rather than definitive misclassification.

Receiver Operating Characteristic Analysis

ROC analysis demonstrated excellent discriminatory performance of attenuation values between infarct stages.

For differentiation of acute and subacute infarcts, a threshold value of 24 HU yielded high diagnostic accuracy, with an area under the curve (AUC) of approximately 0.93.

For differentiation of subacute and chronic infarcts, a threshold value of 14.25 HU demonstrated strong discrimination, with an AUC of approximately 0.95.

These findings indicate robust stage-wise separation using quantitative attenuation thresholds.

ROC analysis was performed using individual attenuation measurements from all patients in the respective comparison groups.

Discussion

The present study demonstrates that quantitative Hounsfield Unit (HU) analysis on non-contrast CT provides a reliable and reproducible method for temporal staging of ischemic cerebral infarction. A progressive reduction in attenuation values was observed from acute to chronic stages, with statistically significant intergroup differences ($p < 0.001$). The derived percentile-based attenuation intervals, combined with high interobserver agreement and MRI validation, support the clinical applicability of attenuation-based stratification as an objective imaging framework.

Attenuation Evolution and Pathophysiological Basis

The observed stepwise decline in mean attenuation values—25.98 HU in acute, 18.76 HU in subacute, and 11.16 HU in chronic infarcts—reflects the biological progression of ischemic injury. In the acute phase, cytotoxic edema leads to intracellular water accumulation with relatively preserved structural integrity, resulting in modest attenuation reduction. During the subacute stage, breakdown of the blood–brain barrier and vasogenic edema contribute to further extracellular water accumulation and greater attenuation decline. In the chronic phase, tissue necrosis, encephalomalacia, and gliosis result in marked

hypodensity approaching cerebrospinal fluid–like attenuation. The quantitative attenuation trajectory observed in this study aligns with established pathophysiological mechanisms of infarct evolution.

Percentile-Derived Attenuation Intervals

Percentile-based distribution analysis (10th–90th percentile) allowed derivation of stage-specific attenuation intervals: acute (23.7–31 HU), subacute (14.5–24.5 HU), and chronic (8.3–14 HU). The use of percentile intervals rather than absolute minimum–maximum ranges minimized the influence of outliers and enhanced statistical robustness. Although minimal overlap was observed at adjacent stage margins, overall attenuation distributions demonstrated clear stage-wise separation. Such limited overlap likely reflects the continuous biological transition of infarction rather than discrete temporal boundaries, particularly near the 48-hour and 14-day clinical thresholds.

ROC Analysis and Diagnostic Discrimination

Receiver operating characteristic (ROC) analysis further reinforced the discriminative performance of attenuation-based staging. A threshold value of approximately +24 HU demonstrated excellent differentiation between acute and subacute infarcts, with an estimated area under the curve (AUC) of 0.93. Similarly, a threshold of approximately +14.25 HU effectively differentiated subacute and chronic infarcts, yielding an estimated AUC of 0.95. The inclusion of normality assessment, post-hoc testing, and ROC-based discrimination further enhances the statistical robustness of the present analysis. These findings indicate strong stage-wise discrimination and suggest that quantitative attenuation thresholds may serve as clinically meaningful decision-support parameters. The high AUC values support the role of HU measurement as a potential quantitative imaging biomarker for temporal stratification.

Reproducibility and Interobserver Reliability

Objective imaging biomarkers must demonstrate reproducibility to be clinically viable. In this study, attenuation measurements showed excellent interobserver agreement (intraclass correlation coefficient = 0.91), confirming that standardized region-of-interest placement yields consistent results across observers. This high reproducibility reduces reliance on subjective visual assessment and strengthens the potential for integration into routine stroke imaging workflows.

MRI Validation and Biological Concordance

The inclusion of an MRI validation subset significantly enhances the strength of the study. CT-based temporal staging demonstrated concordance with MRI features of infarct evolution in 29 of 32 cases (90.6%). Acute cases corresponded with diffusion restriction on diffusion-weighted imaging, subacute cases demonstrated T2 shine through effect with ADC pseudo-normalization, and chronic cases showed encephalomalacic changes with near CSF signal. The few discordant cases were observed near clinical transition intervals, likely representing biological overlap rather than true misclassification. This multimodal validation supports the biological plausibility and reliability of attenuation-based staging.

Clinical Implications

Rapid temporal classification of ischemic infarction has direct implications for treatment planning, prognostication, and rehabilitation strategies. In many emergency and resource-limited settings, MRI may be unavailable or contraindicated. A quantitative CT-based framework offers a practical alternative for temporal

stratification using a widely accessible modality. The derived attenuation intervals and ROC-based thresholds may enhance diagnostic confidence, reduce observer variability, and support standardized reporting.

Comparison with Existing Literature

While early CT signs of ischemia and attenuation changes during infarct evolution have been described in prior studies, systematic derivation of percentile-based attenuation intervals combined with reproducibility assessment and MRI validation has been limited. The present study contributes to the literature by providing a quantitatively validated and statistically robust staging framework derived from a relatively large cohort.

Strengths of the Study

The strengths of this study include:

A substantial cohort of 254 patients

Standardized three-region attenuation measurement protocol

Percentile-based interval derivation minimizing outlier bias

Statistically significant intergroup comparison ($p < 0.001$)

Excellent interobserver agreement (ICC = 0.91)

MRI validation demonstrating 90.6% concordance

ROC-based evaluation confirming strong discriminatory performance

Collectively, these elements enhance methodological rigor and clinical relevance.

Limitations

Certain limitations should be acknowledged. The retrospective design may introduce selection bias. Temporal classification was based on clinical history, which may be subject to recall variability. Attenuation values may vary with scanner calibration and acquisition parameters, potentially affecting generalizability across institutions. Additionally, ROC estimates were derived from cohort-based distribution analysis rather than prospective external validation. Future multicenter studies with standardized imaging protocols and independent validation cohorts are warranted. Although a standardized imaging protocol was used, attenuation measurements may vary across different CT platforms and calibration settings, which may influence external reproducibility.

Future Directions

Prospective validation across multiple institutions, integration of automated attenuation mapping tools, and combination with advanced quantitative imaging techniques may further refine attenuation-based staging. Incorporation of machine learning algorithms using HU distributions could potentially enhance diagnostic precision and individualized stroke assessment.

Conclusion

Quantitative Hounsfield Unit analysis on non-contrast computed tomography provides an objective, reproducible, and clinically applicable method for temporal staging of ischemic cerebral infarction. A progressive reduction in attenuation values was observed across acute, subacute, and chronic stages, with statistically significant differentiation and strong discriminatory performance on receiver operating characteristic analysis. The derived percentile-based attenuation intervals demonstrated clear stage-wise separation, supported by excellent interobserver reliability and high concordance with magnetic resonance imaging validation.

These findings suggest that attenuation-based stratification may serve as a practical reference framework for CT-based temporal classification, particularly in emergency and resource-limited settings

where advanced imaging modalities are unavailable or contraindicated. Further multicenter validation may strengthen its generalizability and support broader clinical implementation. Prospective multicenter validation across diverse imaging platforms may further establish the generalizability of attenuation-based temporal classification.

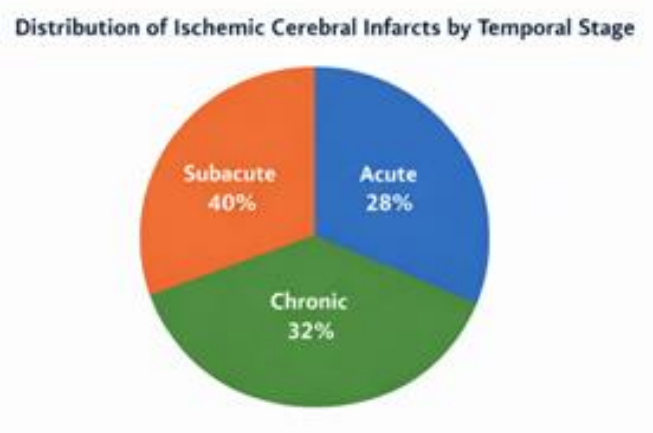

Figure 1: Distribution of ischemic cerebral infarcts by temporal stage.

Pie chart illustrating the proportion of acute (28%), subacute (40%), and chronic (32%) ischemic cerebral infarcts in the study cohort of 254 patients.

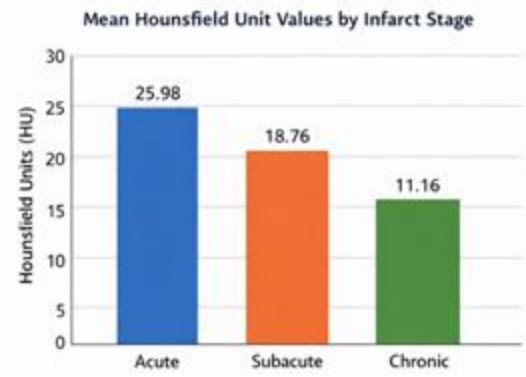

Figure 2: Mean attenuation values across infarct stages

Bar graph demonstrating progressive reduction in mean Hounsfield Unit (HU) values from acute (25.98 HU) to subacute (18.76 HU) and chronic (11.16 HU) stages of ischemic cerebral infarction.

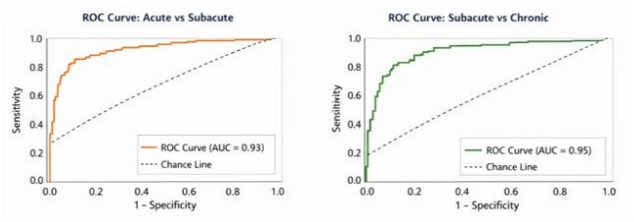

Figure 3: Receiver operating characteristic analysis of attenuation-based stage differentiation

(A) ROC curve demonstrating differentiation between acute and subacute infarcts (AUC = 0.93).

(B) ROC curve demonstrating differentiation between subacute and chronic infarcts (AUC = 0.95).

Both curves indicate excellent discriminatory performance of quantitative attenuation thresholds.

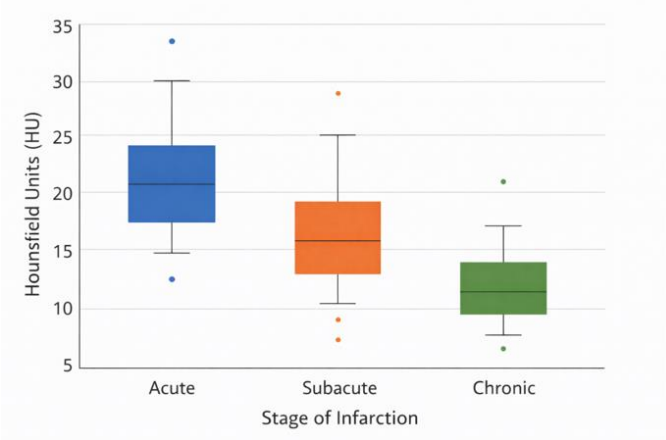

Figure 4: Distribution of attenuation values across infarct stages

Box-and-whisker plot demonstrating the distribution of Hounsfield Unit (HU) values across acute, subacute, and chronic ischemic cerebral infarction stages. The boxes represent the interquartile range (25th–75th percentile), the central line indicates the median value, and the whiskers extend to the minimum and maximum values excluding outliers. Progressive reduction in attenuation values is observed from acute to chronic stages, with limited overlap between adjacent groups.

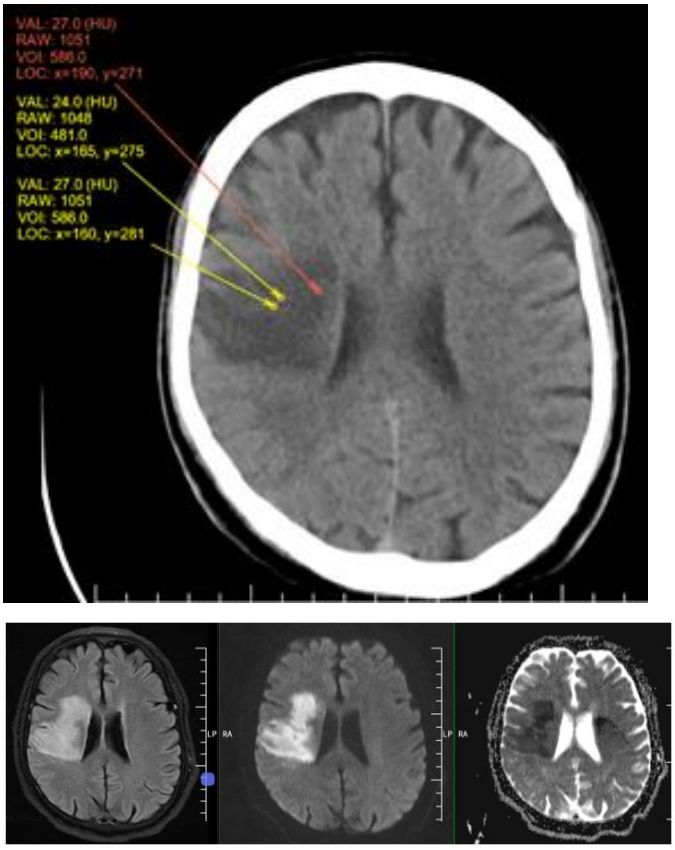

Figure 5: Representative acute ischemic infarction with CT attenuation measurement and MRI correlation

(A) Axial non-contrast CT image in a patient presenting with 8 hours of acute onset left sided weakness, demonstrating wedge shaped parenchymal hypodensity. Three standardized circular regions of interest (ROIs) within the infarcted region show attenuation values of 27 HU, 24 HU, and 27 HU (mean ≈ 26 HU), consistent with acute-stage infarction.

(B to D) Corresponding MRI sequences demonstrate FLAIR hyperintensity, diffusion restriction on diffusion-weighted imaging, and low signal on apparent diffusion coefficient map, confirming acute ischemic infarction.

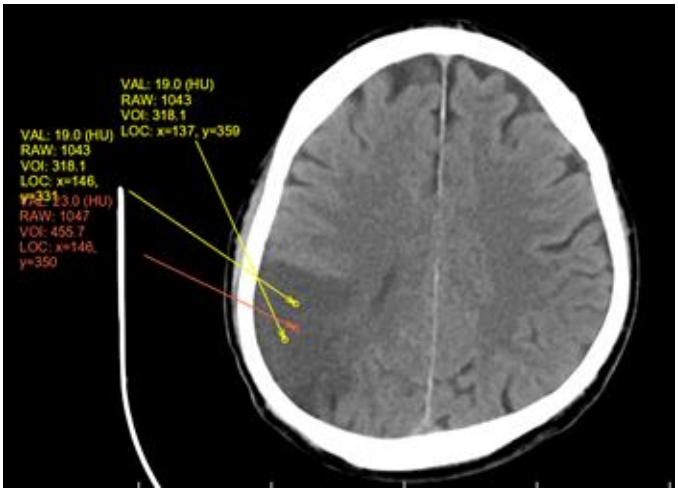

Figure 6: Representative subacute ischemic infarction on CT

Axial non-contrast CT image in a patient presenting with 3 days of neurological deficit, demonstrating well-defined hypodensity consistent with subacute infarction. Three standardized circular regions of interest (ROIs) show attenuation values of 19 HU, 19 HU, and 23 HU (mean ≈ 20 HU). Subsequent MRI demonstrated FLAIR hyperintensity with evolving diffusion characteristics on DWI and relative ADC pseudo-normalization, consistent with subacute infarct evolution.

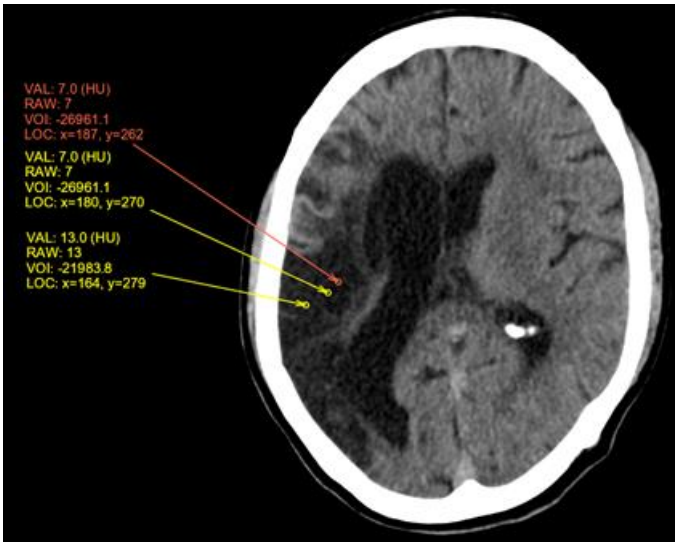

Figure 7: Representative chronic ischemic infarction in the right frontal-parietal lobe

Axial non-contrast CT image in a patient with a history of remote neurological deficit and prior stroke episode three to four weeks earlier, demonstrating large confluent hypodensity with associated parenchymal volume loss in the right frontal-parietal lobe, consistent with chronic infarction. Three standardized circular regions of interest (ROIs) within the lesion show attenuation values of 7 HU, 7 HU, and 13 HU (mean ≈ 9 HU), corresponding to chronic-stage infarct evolution.

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