Hematoma expansion prediction in patients with intracerebral hemorrhage using a deep learning approach

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Background: Intracerebral hemorrhage (ICH) constitutes a life-threatening medical emergency characterized by a high mortality rate. The precise prediction of hematoma expansion (HE) in individuals with ICH is crucial for guiding clinical decision-making. However, we lack a standardized automated system that harnesses artificial intelligence for the timely and accurate prediction of HE in ICH cases, particularly when non-contrast computed tomography (NCCT) imaging is employed in emergency settings. Therefore, we developed a deep learning-based methodology NCCT for the purpose of HE prediction.

Methods: Our deep learning model automatically segments ICHs and stratifies them using NCCT data. We comprehensively investigated various input methods and deep learning algorithms to enhance the predictive performance of our model.

Results: The model demonstrated a competitive performance, with a notable improvement evident when using volumetric NCCT data and emphasizing slices containing hemorrhagic regions. Among established deep learning algorithms, the modified Swin-UNETER model emerges as a promising performer (accuracy: 0.74, precision: 0.76, and specificity: 0.90).

Conclusions: Collectively, we present a novel approach to HE in patients with ICH by employing deep learning and NCCT data. The capacity of the model for automated ICH segmentation and its improved predictive accuracy with volumetric NCCT data highlight its potential clinical utility. These findings contribute to advancing early HE prediction and providing valuable insights to enhance patient care and outcomes.

Keywords: Hematoma expansion (HE); intracerebral hemorrhage (ICH); deep learning; non-contrast computed tomography (NCCT); Swin transformer

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Introduction

Intracerebral hemorrhage (ICH) comprises approximately 10–20% of all stroke cases, with nearly 40% of ICH patients succumbing within the initial month. Only 12–39% of survivors achieve sustained functional independence in the long term (1). The prevention of hematoma expansion (HE) is widely recognized as an effective therapeutic approach in managing ICH. Numerous techniques have been investigated for their ability to prevent HE, many of which rely on rapidly detecting patients displaying signs of HE (2). Some imaging phenomena have been associated with

HE. One such phenomenon is the computed tomography angiography (CTA) spot sign, denoting the presence of single or multiple areas with contrast enhancement within the hematoma. This sign helps predict HE with a sensitivity ranging from 51–62% and a specificity ranging from 85–88% (3,4). Nevertheless, its clinical application is constrained owing to limited CTA use. Consequently, several studies have aimed to identify imaging markers using non-contrast computed tomography (NCCT). Factors such as a large initial volume, irregular shape, and heterogeneous composition of the hematoma have been recognized as indicators of HE (5-7). However, ensuring the accuracy of these indicators is challenging unless a trained professional conducts the analysis, especially in urgent situations such as those observed in emergency rooms. Recent advancements in artificial intelligence (AI) have enabled its integration into medical image analysis, potentially offering substantial assistance in image interpretation, particularly in urgent settings like emergency departments. Hence, the development of automated AI models holds significant promise for enhancing emergency care.

Accordingly, in this study, we evaluated multiple AI algorithms in conjunction with different variations of the hematoma mask and subsequently proposed an optimized AI algorithm for HE prediction.

Highlight box

Key findings

- Deep learning-based methodology using on non-contrast computed tomography (NCCT) may have the potential clinical utility of predicting hematoma expansion (HE), enhancing patient care outcomes.
- Deep learning-based model exhibits competitive performance when utilizing volumetric NCCT data and emphasizing slices containing hemorrhagic regions.
- Swin-UNETER model is a promising performer among the deep learning algorithms with notable accuracy, precision, and specificity metrics.

What is known and what is new?

- Computed tomography angiography (CTA) spot sign has been recognized to be associated with HE. NCCT also provides informative indicators such as the "blend sign", "black hole sign", and "island sign". Recent advancements in machine learning and deep learning methodologies have facilitated the prediction of HE.
- Our investigation explores the optimization of predictive performance through the examination of various input methods and deep learning algorithms. We found that utilizing volumetric NCCT data, with a specific emphasis on slices containing hemorrhages, significantly enhances the predictive capabilities of the model and the modified Swin-UNETR model is a promising performer among well-known deep learning classification algorithms.

What is the implication, and what should change now?

- The development of deep learning models for predicting HE enables the stratification of intracerebral hemorrhage (ICH) patients. This advancement holds significant implications for clinical practice, as clinicians can now identify ICH patients at high risk for HE more accurately.

Methods

Data preparation

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Gangnam Severance Hospital Institutional Review Board (No. 3-2022-0098), which waived the requirement for informed consent, because of retrospective design. We retrospectively searched electronic medical records to identify patients with spontaneous ICH who underwent NCCT between March 2013 and April 2022. We included patients with following characteristics: primary spontaneous ICH with baseline volume ≤60 mL (8), presentation to the emergency department within 6 hours from symptom onset, availability of baseline and follow-up NCCT data within 48 hours after symptom onset, and the absence of anticoagulant treatment. Exclusion criteria included secondary ICH, hemorrhagic transformation of ischemic stroke, primary intraventricular hemorrhage, and NCCT images of insufficient quality.

Image acquisition and analysis

All NCCT scans were performed using a 128-slice multi-detector CT system (SOMATOM Definition AS+; Siemens Healthcare, Erlangen, Germany). Imaging parameters included a collimation of 64 mm × 0.6 mm, slice acquisition of 128 mm × 6 mm using a z-flying focal spot technique, a gantry rotation time of 0.5 s, a pitch of 0.45, and an exposure setting of 120 kVp and 140 mAs_{eff} with automatic tube current modulation (CARE Dose 4D). ICH hyperdensity was manually traced by a radiologist with 8 years of clinical experience on each two-dimensional slice of each three-dimensional CT image stack using open-source software ITK-Snap, version 3.8.0 (available at www.itksnap.org). Another neuroradiologist with 14 years of clinical experience confirmed the presence of segmented ICHs and

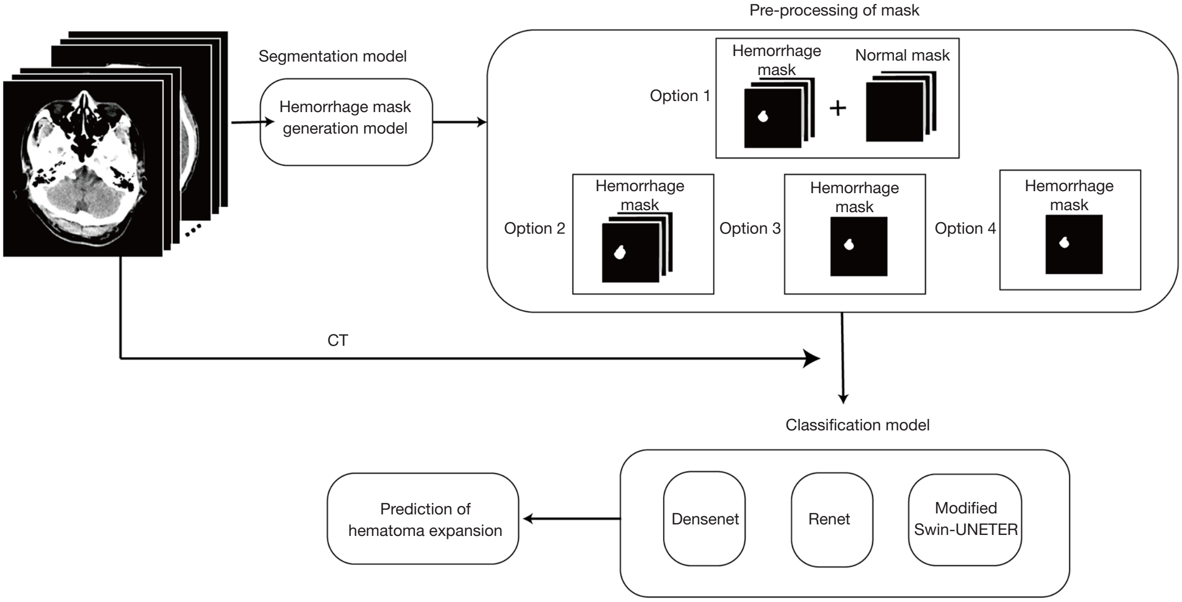

Figure 1 System architecture for prediction of hematoma expansion. CT, computed tomography.

resolved ambiguous cases. These manual segmentations of ICH on baseline and follow-up NCCT were used to calculate ICH volume and define HE. Also, it was used as a test set to assess the performance of predeveloped ICH segmentation model (Figure S1). ICH volumes were calculated by multiplying the number of segmented voxels (volumetric pixels) by the distance between each voxel in the x-, y-, and z-dimensions. HE was defined as relative hematoma growth >33% or absolute hematoma growth >6 mL from baseline hemorrhage volume (9).

System architecture

Our deep learning architecture comprises a two-output model for predicting early HE (*Figure 1*). We employed a predeveloped segmentation model, and its performance in our cohort is detailed in Table S1. Our segmentation model generated a hemorrhagic mask highlighting the hemorrhagic regions in the brain. The classification model utilized both the original NCCT scan data and the generated hemorrhagic mask as inputs for predicting early HE. To optimize our approach, we explored four variations of the original NCCT data: (I) complete NCCT slices; (II) slices containing hemorrhage; (III) a single slice with the largest gap in attenuation within the hemorrhagic region; and (IV) a single slice with the largest area of hemorrhage. Additionally, we evaluated the performance of three classification models, namely, DenseNet (10), ResNet (11), and modified Swin-UNETER (12), to develop a HE model with optimal performance. ResNet employs preceding features with an identity shortcut to achieve excellent performance (Figure S2). DenseNet utilizes dense concatenation for all subsequent layers to avoid using direct summation and preserve features in the preceding layers (Figure S3). We modified the Swin-UNETR, which has a U-shaped network design utilizing a Swin transformer as the encoder and a convolutional neural network (CNN)-based decoder connected to the encoder through skip connections at different resolutions (*Figure 2*). The patients were randomly divided into training and test sets in a 4:1 ratio.

Statistical analysis

Differences in clinical characteristics of patients were calculated using Student's *t*-test or Mann-Whitney *U*-test. Differences in categorical variables were estimated using the chi-squared test. To compare the performance of deep learning algorithms for hematoma prediction, we assessed accuracy, precision, sensitivity, and specificity. The classification tasks involved binary classifications, with the threshold set at 0.5.

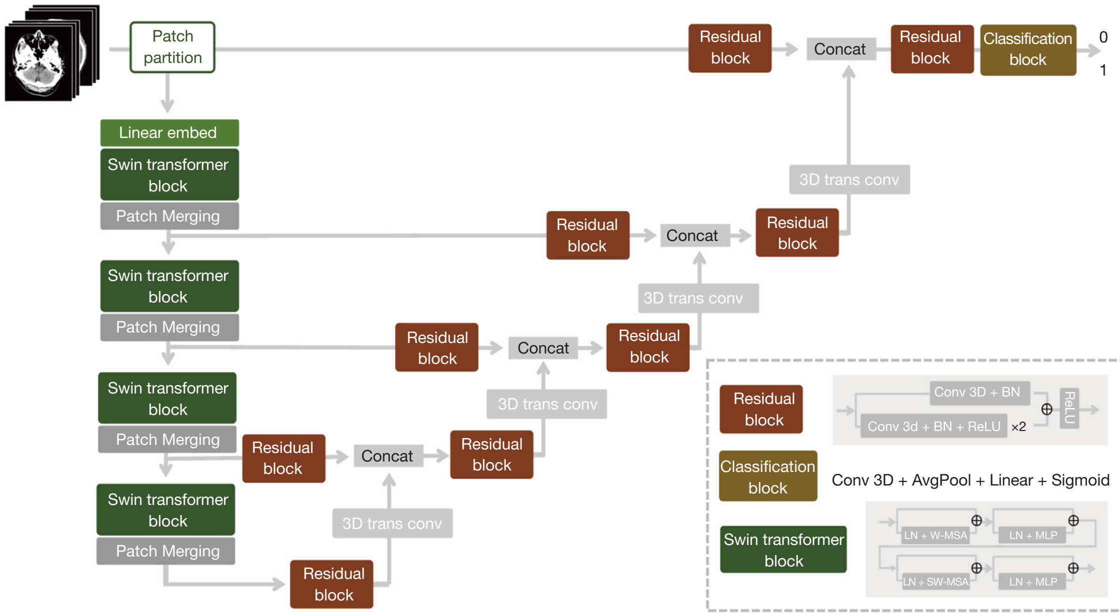

Figure 2 Structure of the modified Swin UNEt TRansformers (Swin-UNETR). Swin Transformer inputs feature maps into the encoder blocks, sequentially passing through LayerNorm (LN) layer, W-MSA, multiple-layer perceptions (MLP) layer, SW-MSA, and MLP layer. W-MSA and SW-MSA are multi-head Self-Attention modules with regular and shifted windowing configurations, respectively.

Table 1 Patient characteristics grouped into training and test sets

Variables	Training set (N=197)	Test set (N=50)	P value
Gender, male	127 (64.5)	31 (62.0)	0.82
Age, years	58.3±13.8	60.1±12.9	0.42
Baseline hematoma volume, mL	15.6±12.8	16.9±15.3	0.14
Hematoma expansion	79 (40.1)	20 (40.0)	0.91

Data are n (%) or mean ± standard deviation.

Results

A total of 247 patients met the inclusion criteria. Baseline patient characteristics were compared between the training and test datasets (*Table 1*). We observed no significant differences between the training and test datasets in terms of sex, age, baseline hematoma volume, or the percentage of HE. HE was observed in 40% of patients (99/247). The performance of the classification models, in conjunction with different mask variations, is summarized in *Table 2*. The modified Swin-UNETR model, using slices with hemorrhage as masks, demonstrated the highest accuracy (0.74), precision (0.76), and specificity (0.90). The DenseNet model, using the slice with the largest hemorrhagic area as the mask, exhibited the highest sensitivity (0.7).

Discussion

ICH ranks among the most frequent causes of emergency room visits and is a grave condition with a hospital mortality rate of 40–50% (8,13). While standard treatment guidelines for ICH remain elusive, consensus prevails in many studies regarding the grim prognosis associated with HE, emphasizing the need for heightened surveillance and timely treatment. Consequently, several studies have focused on the early detection of HE (14-16). In this study, we developed a deep learning approach based on NCCT to predict HE in patients with ICH. Our model demonstrated the ability to automatically segment ICHs and stratify them, performing reasonably compared with existing prediction models or NCCT markers. We explored

Table 2 Performance of different prediction models on the validation set

Input	Classification model	Accuracy	Precision	Sensitivity	Specificity
Complete slices of NCCT + hemorrhagic mask	Densenet-3D	0.66	0.57	0.55	0.73
	Modified Swin-UNETER	0.62	0.53	0.40	0.76
	ResNet-50	0.68	0.62	0.50	0.80
	ResNet-18	0.66	0.66	0.30	0.90
Slices with hemorrhage + hemorrhagic mask	Densenet-3D	0.70	0.64	0.55	0.80
	Modified Swin-UNETER	0.74*	0.76*	0.50	0.90*
	ResNet-50	0.70	0.63	0.60	0.76
	ResNet-18	0.58	0.47	0.50	0.63
A single slice with the largest gap in attenuation within hemorrhage + hemorrhagic mask	Densenet-2D	0.62	0.52	0.50	0.70
	Modified Swin-UNETER	0.60	0.50	0.60	0.60
	ResNet-50	0.68	0.62	0.50	0.80
	ResNet-18	0.70	0.64	0.55	0.80
A single slice with the largest area of hemorrhage + hemorrhagic mask	Densenet-2D	0.68	0.58	0.70*	0.66
	ResNet-50	0.64	0.55	0.55	0.70

Asterisk (*) indicates the highest value in metrics of classification performance. NCCT, non-contrast computed tomography.

various input methods and deep learning algorithms to optimize their performance. Our investigation revealed that using volumetric NCCT data, with an emphasis on slices containing hemorrhages, could enhance the predictive capabilities of the model. Furthermore, among well-known deep learning classification algorithms, the results from the modified Swin-UNETR model showed promise.

Early research identified significant markers on both CTA and NCCT relevant to the prediction of HE. For example, the CTA spot sign demonstrated approximately 60% sensitivity and 90% specificity for predicting HE (4,17). Additionally, detecting signs of leakage and heightened iodine concentrations within the spot signs can increase sensitivity (18). Notably, contrast agents used in imaging can adversely affect renal function, rendering NCCT a more accessible option than CTA for preliminary intracranial hemorrhage assessment. NCCT provides informative indicators such as the "blend sign", indicating a hematoma with hyper- and hypodense areas, and the "black hole sign", indicating a hypodense area within a hyperdense area. These signs were significant with a predictive specificity of approximately 90% (19,20). Another noteworthy NCCT marker for HE is the "island sign", signifying the presence of multiple small hematomas either separate from or connected to the main hematoma (*Figure 3*). This sign independently predicts HE and poor outcomes in patients with ICH (21). However, all the NCCT markers mentioned exhibit relatively low sensitivity levels (approximately 40%), posing practical challenges in clinical use. Recently, radiomics models have emerged with the assistance of machine-learning technology, showcasing promising results in HE prediction with areas under the curve (AUCs) ranging from 0.73–0.89 (22-24). Nevertheless, manual segmentation of hematomas, required for these radiomic models, could limit their practical application. As an alternative, a deep learning method has been developed to predict HE in patients with ICH, achieving an average AUC of 0.78 (25). In clinical settings, the value of magnetic resonance imaging (MRI) imaging in predicting HE is limited. MRI holds promise for evaluating underlying etiologies contributing to ICH, such as cerebral amyloid angiopathy, arteriovenous shunting, and brain tumors (26,27). However, it is important to consider that MRI scans typically require a longer acquisition time and are relatively expensive compared to other imaging modalities. Therefore, its role in predicting HE in ICH patients warrants further investigation.

However, the performance of deep learning-based algorithms can be affected by the chosen input approach, including options such as using a single representative CT

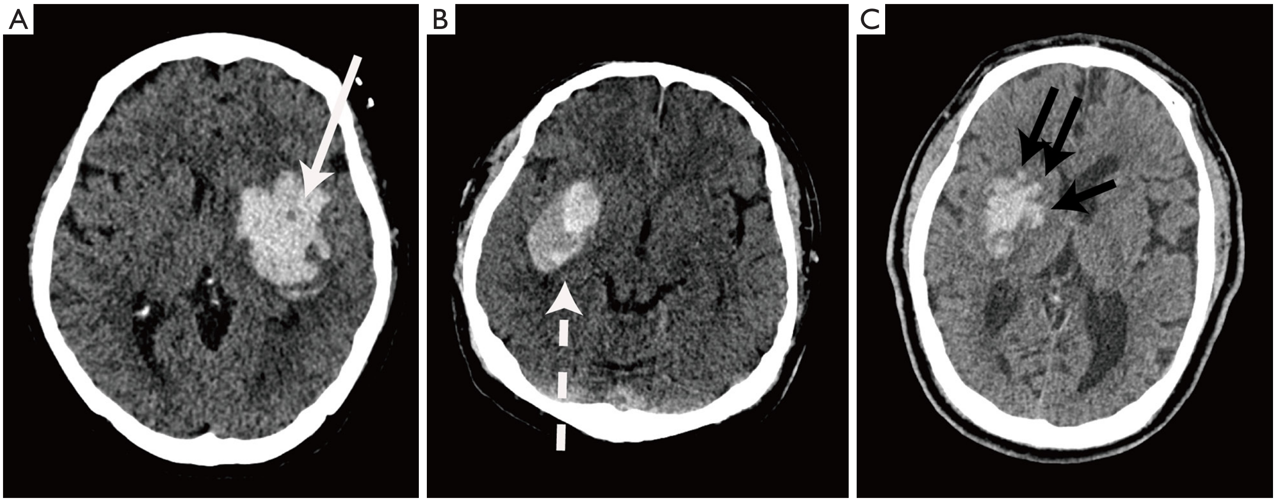

Figure 3 Representative examples of NCCT markers of HE. (A) Black hole sign refers to the round, oval, or rod-shaped relatively hypoattenuated area (white arrow) inside the hyperattenuated hematoma with a clear border to nearby brain tissue. (B) Blend sign refers to the blending of hyperattenuating region with adjacent relatively hypoattenuating area (dotted arrow) with a well-defined margin. (C) Island sign refers to three or more scattered small hematoma detached from the main hematoma, or more than 4 small hematoma connected partly or wholly with the main hematoma (black arrows). NCCT, non-contrast computed tomography; HE, hematoma expansion.

slice, employing volumetric CT data, prioritizing pre-emphasized hemorrhagic regions, or considering unbiased information. Our findings indicate that an algorithm trained using volumetric data outperforms one using only a single representative slice. One potential explanation is that the algorithm trained on volumetric data benefits from information across all slices containing hemorrhages, whereas a single CT image captures details from a single cross-section of the hemorrhage. In this specific slice with the largest hemorrhage area essential features indicative of HE may be missed. Furthermore, within the category of volumetric data, the algorithm that employs a constrained set of volumetric data, comprising solely slices with hemorrhage, and thus emphasizing hemorrhagic regions, exhibited superior performance compared with that using unbiased volumetric data across the entire set. The restriction of volumetric data solely to the hemorrhage area enables the algorithm to focus on the critical region of interest while mitigating noise. Consequently, this approach significantly enhances overall performance (28,29).

Recently, transformer-based models have gained prominence owing to their ability to capture long-range dependencies, effectively overcoming limitations associated with a fixed kernel size in CNN-based techniques (30,31). Vision transformers (ViTs) are renowned in computer vision for their state-of-the-art performance (32,33). A recent addition to this domain is the Swin transformer, a hierarchical vision transformer capable of self-attention through an efficient shifted window-partitioning scheme (34). Swin transformers are versatile across various downstream tasks and outperform previous models (11,30). In the context of medical image analysis, Swin-UNETR transformers (Swin-UNETR) employ a U-shaped network structure featuring a Swin transformer as an encoder, connected to a CNN-based decoder operating at different resolutions through skip connections (12). The capacity for long-range dependencies and self-attention within our modified Swin-UNETR model could be a contributing factor to its superior performance compared with that of CNN-based models such as DenseNet or ResNet.

According to our results, the DenseNet model using a single slice with the largest area of hemorrhage exhibited the highest sensitivity, while the Swin-UNETR model had the highest accuracy, precision, and specificity. Based on these distinct performance metrics, DenseNet can serve as an effective screening tool in clinical practice. For instance, if DenseNet indicates a likelihood of hematoma expansion in patients, clinicians may opt to hospitalize them for a longer duration and institute closer monitoring protocols to promptly detect any signs of worsening. Conversely, given that the Swin-UNETR model exhibits the highest specificity, clinicians may lean towards considering more invasive treatment options, such as hematoma evacuation, for patients identified as having a high probability of hematoma expansion by this model. This underscores the importance of leveraging the strengths of each model in clinical decision-making, depending on the specific context and objectives of patient care (35).

Our study has several limitations. First, this was a retrospective study conducted at a single center, limiting the generalizability of our model. Multicenter validation is necessary to enhance the robustness of our model's predictions. Second, our current model exclusively incorporates imaging data, and its performance could potentially be improved by incorporating additional clinically significant features obtained from a comprehensive analysis of patient clinical data.

Conclusions

Despite these limitations, our deep learning model based on NCCT effectively segmented and stratified ICHs. Our findings emphasize the advantages of using volumetric NCCT data, particularly with a focus on slices containing hemorrhagic regions, which significantly enhances predictive accuracy. Furthermore, our findings highlight the potential of the modified Swin-UNETR model among well-established deep learning algorithms as a promising performer. Collectively, our novel model aids in the accurate prediction of HE in patient with ICH, thereby paving way for its early identification and intervention, potentially improving patient outcomes and enhancing the management of this life-threatening condition.

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Footnote

Data Sharing Statement: Available at https://jmai.amegroups.com/article/view/10.21037/jmai-24-5/dss

Peer Review File: Available at https://jmai.amegroups.com/article/view/10.21037/jmai-24-5/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jmai.amegroups.com/article/view/10.21037/jmai-24-5/coif). H.N., S.J., S.L., J.J. are employed by SK C&C. S.J.A. received funding from a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI20C2125). The other author has no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Gangnam Severance Hospital Institutional Review Board (No.: 3-2022-0098), which waived the requirement for informed consent, because of retrospective design.

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Supplementary

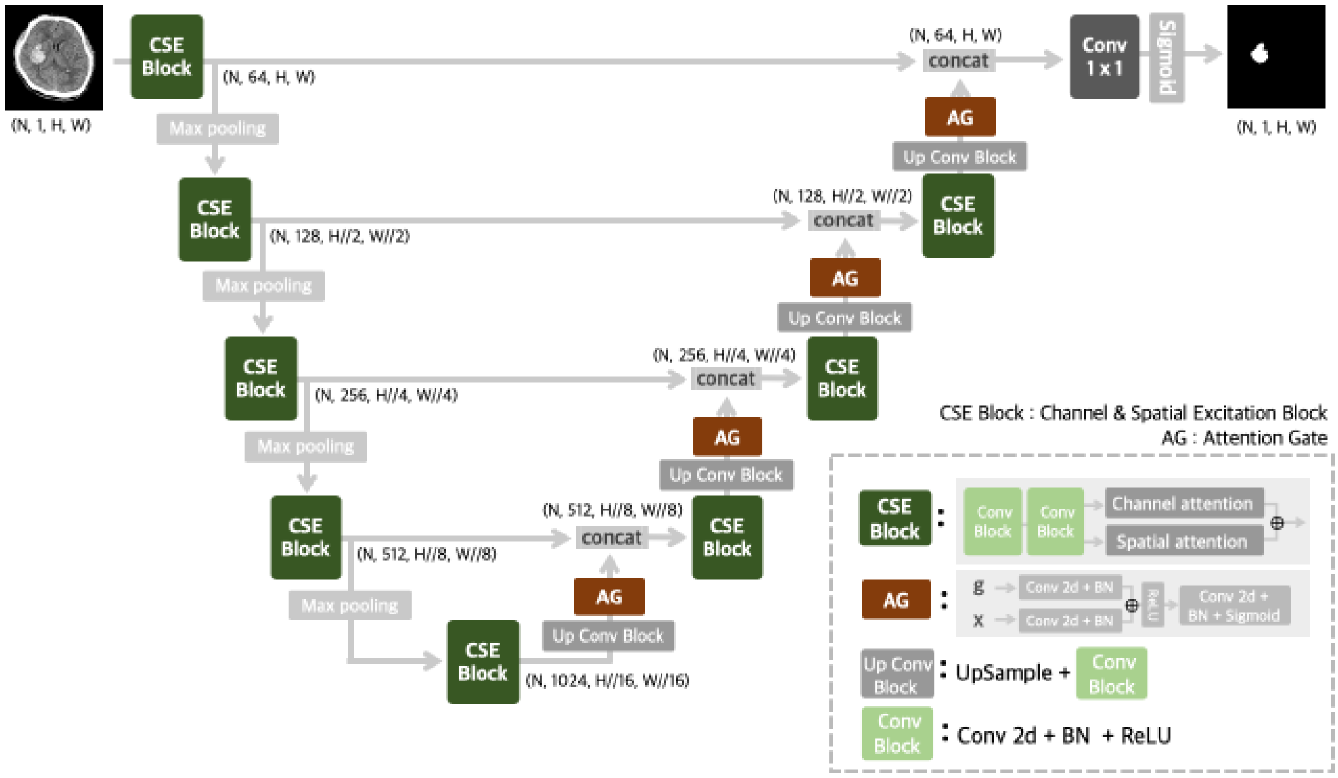

Figure S1 AGCSE-Net model structure.

Table S1 Detection and segmentation performance of AGCSE-Net model in our cohort

	Detection				Segmentation
	Accuracy (%)	Precision (%)	Sensitivity (%)	Specificity (%)	DSC
AGCSE-Net	91.0	70.6	94.8	90.0	0.75

DSC, Dice score coefficient.

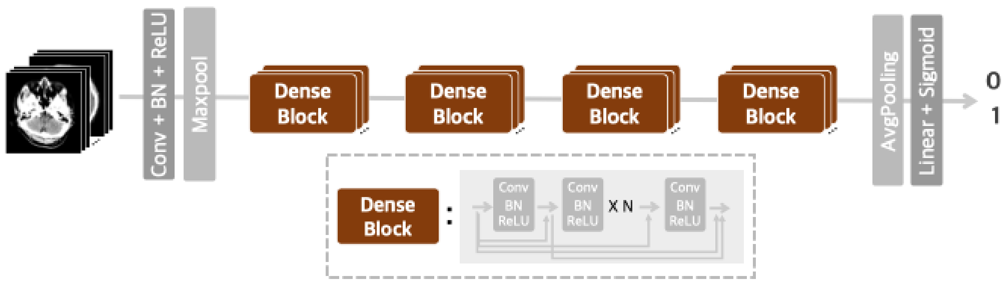

Figure S2 Structure of DenseNet.

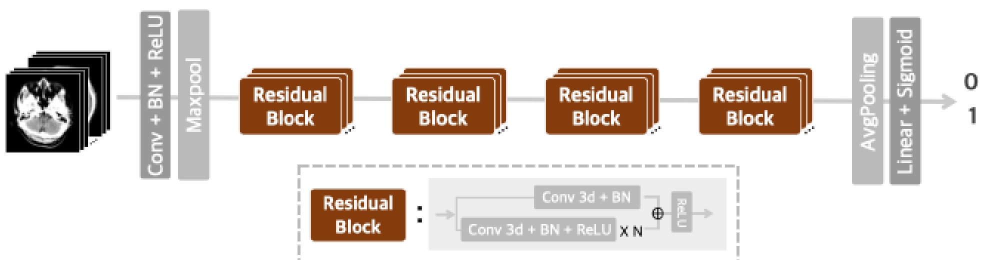

Figure S3 Structure of ResNet.

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