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² Automatic detection of ischemic stroke using higher order ³ spectra features in brain MRI images

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18 Abstract

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 The gravity of ischemic strokes is the key factor in deciding upon the optimum therapeutic intervention. Ischemic strokes can be divided into three main groups: lacunar syndrome (LACS), partial anterior circulation syndrome (PACS), and total anterior circulation stroke (TACS), where the corresponding severity is mild, medium, and high, respectively. Herein, a unique method for the automatic detection of ischemic stroke severity is presented. The proposed system is based upon the extraction of higher order bispectrum entropy and its phase features from brain MRI (Magnetic Resonance Imaging) images. For classification, which is used to establish stroke sever- ity, a support vector machine was incorporated into the design. The developed technique effectively detected the stroke lesion, and achieved a sensitivity, specificity, accuracy, and positive predictive value equal to 96.4%, 100%, 97.6% and 100%, respectively. The results were obtained without the need for manual intervention. This design is advantageous over state-of-the-art automated stroke severity detection systems, which require the reading neuroradiologist to manually determine the region of interest. Hence, the method is effica- cious for delivering decision support in the diagnosis of ischemic stroke severity, thereby aiding the neuroradiologist in routine screening procedures.

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32 Keywords: Ischemic stroke; Entropy; Bispectrum; Classifier; ADASYN; HOS

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1. Introduction 34

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Ischemic stroke results from a lack of blood supply to a 35 specific region of the brain ([Fig. 1](#page-3-0)). This diminishes the 36 basic functions of nerve cells in the affected brain area, 37 and can lead to significant long-term disability. Stroke is 38

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Ischemic Stroke

Fig. 1. Illustration of ischemic stroke.

 a worldwide issue, being the second leading cause of death and the third leading cause of disability ([Bonita, 1992\)](#page-9-0). Ischemic strokes can be grouped into one of three types [\(Lindgren, Norrving, Rudling, & Johansson, 1994](#page-10-0)):

- 43 1. Partial anterior circulation syndrome (PACS): the mid-44 dle/anterior cerebral regions are affected due to this type 45 of stroke.
- 46 2. Lacunar syndrome (LACS): this stroke results from the 47 occlusion of vessels that provide blood to the deep brain 48 regions;
- 49 3. Total anterior circulation stroke (TACS): middle/ante-50 rior cerebral regions are affected due to a massive brain 51 stroke.

 [Osmani, Durrani, and Ara \(2010\)](#page-10-0) compared the out- come in these three different types of stroke. A chi- squared test was employed to compare proportion differ- ence in results across the different types strokes, with p ≤ 0.05 considered to be statistically significant. They established that TACS has the worst outcome with the highest number of mortalities, whereas LACS had a better outcome. To be specific, a majority of LACS patients were functionally independent after 6 months. The patients with PACS had an average outcome, better than those with TACS, but not as positive as those with LACS.

 In order to decide upon therapeutic intervention, the diagnosis, along with the severity of the ischemic stroke, are of fundamental importance ([Zaidi, 2012](#page-10-0)). MRI images contain salient information for classification of ischemic stroke severity. However, the scan results are difficult to analyze, because subtle changes in the images are the points that are indicative of stroke severity. This difficulty translates into a long time spent in manual image analysis. 71 Executing the mental tasks necessary to establish stroke 72 severity causes fatigue, and in turn fatigue may lead to 73 human error, which lowers diagnostic quality. Apart from 74 fatigue, inter- and intra-observer variability exists for all 75 human-based classification methodology. Education of 76 the clinical analyst is a tool that can partially ameliorate 77 these pitfalls. Yet, training a person to the expert level is 78 time consuming and expensive, which makes routine stroke 79 risk estimation tasks uneconomical. 80

Scientists and engineers have addressed these problems 81 by developing reliable methods for the automatic detection 82 of ischemic stroke severity. Recent research focuses on 83 design systems which aid reading neuroradiologists by 84 reducing both the amount and duration of routine tasks. 85 Numerous studies in the literature focus on the diagnosis 86 of ischemic stroke in magnetic resonance imaging (MRI) 87 of the brain. Among the various MRI imaging modalities, 88 diffusion weighted imaging (DWI) is quite sensitive to small 89 water diffusion changes in the acute ischemic brain, and is 90 therefore often used for timely stroke detection ([Lutsep](#page-10-0) 91) [et al., 1997; Newcombe, Das, & Cross, 2013\)](#page-10-0). Many previ- 92 ous ischemic stroke classification methods were based upon 93 an intimal segmentation of the brain lesion within the 94 image, ranging from the use of simple edge-based and 95 threshold-based methods ([Carson, Belongie, Greenspan,](#page-9-0) 96 [& Malik, 2002; Wang, Xiang, Pan, Wang, & Meng,](#page-9-0) 97 [2013\)](#page-9-0) to clustering-based and supervised methods ([Ji,](#page-10-0) 98 [Xia, & Zheng, 2017; Sridevi & Mala, 2019\)](#page-10-0) to methods 99 based on Delaunay triangulation ([Subudhia, Dash, Jena,](#page-10-0) 100 [& Sabut, 2018\)](#page-10-0). The downside to these techniques is that, 101 since the segmentation is the first stage of the entire classi- 102 fication process, an inaccurate segmentation of the brain 103 lesion, within the DWI image, percolates throughout the 104 processing chain. As a result, even small variations during 105 image segmentation have a disproportionally large effect 106 on ischemic stroke classification. Prior studies have sup- 107 posed perfect image segmentation, which is difficult to 108 achieve in practice. Thus, the possibility of an imperfect 109 image segmentation is expected to have a negative impact 110 on ischemic stroke classification quality in a practical 111 setting. 112

Artificial intelligence techniques have been used in med-
113 ical applications to predict diseases and the outcome in 114 ischemic stroke patients ([Scalzoa et al., 2013](#page-10-0)). [Ramli,](#page-10-0) 115 [Ghazali, and Tay \(2018\)](#page-10-0) employed three emboli detection 116 techniques; the sinusoidal model, energy and zero crossing 117 rate and short time average zero crossing rate to examine 118 the spectrum of high magnitude frequency element. Sinu- 119 soidal modelling yielded the highest accuracy of 84.2% 120 for the classification of ischemic stroke. [Chin, Lin, Wu,](#page-9-0) 121 [Weng, Yang, and Su \(2017\)](#page-9-0) developed a network using 122 deep learning algorithms, to classify ischemic stroke auto- 123 matically and obtained an accuracy of more than 90%. 124 Many other methods have also been deployed using 125

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 machine learning to confront issues of lesion segmentation and/or classification ([Feng, Zhao, & Huang, 2016;](#page-10-0) [Hemanth, Vijila, Selvakumar, & Anitha, 2013; Hevia-](#page-10-0) [Montiel, 2007; Mitra, 2014\)](#page-10-0), and yet, the majority of tech- niques still depend strongly upon a first accurate segmenta-tion of the lesion.

 Recently, higher order spectra (HOS) methods have been effectively used to pick the minute details in the sig- nals and images [\(Martis, Acharya, Mandana, Ray, &](#page-10-0) [Chakraborty, 2013; Noronha, Acharya, Nayak, Martis,](#page-10-0) [& Bhandary, 2014; Swapna, Rajendra Acharya,](#page-10-0) [Vinithasree, & Suri, 2013\)](#page-10-0). The bispectrum entropy and phase features have been effectively used in many applica- tions, such as in cardiac decisions ([Martis et al., 2013\)](#page-10-0), the diagnosis of fatty liver disease and cirrhosis [\(Acharya](#page-9-0) [et al., 2015; Acharya, 2016](#page-9-0)), and in thyroid nodule severity diagnosis ([Raghavendra, 2018](#page-10-0)).

 In this study, we aim to provide an automatic detection of ischemic stroke severity using machine learning tech- niques, without employing any segmentation method that relies upon the calculation of higher-order bispectrum entropy features on the input DWI image, overcoming the problems that can derive from inaccurate lesion segmentation.

150 2. Materials and methods

 This section introduces the materials and methods used to develop the proposed stroke severity classification sys- tem. The basic idea behind the system design is to find dis- criminative features which extract diagnostically relevant information from DWI images. Feature extraction is neces- sary, because the machine learning algorithms, in our case the SVM, cannot readily address high dimensional data, such as is typically found in biomedical imagery. The fea- ture extraction projects the image into a lower dimensional space, which is then input to a machine classifier. Fig. 2 provides an overview block diagram of the system. The subsequent sections introduce the functionality of the indi-vidual blocks.

164 2.1. Image database

 The dataset used in this study was obtained from stroke patients at the IMS and SUM Hospital, Bhubaneswar, Odisha, India, and each patient had a prominent visible stroke lesion evident within the image. All images were acquired with Signa HDxT 1.5 T Optima Edition (GE Healthcare, Waukesha, WI) and were exported for offline processing. The ethics committee approved the study, and the patients signed an informed consent before to being included. The image database consisted of 267 brain 173 MRI images using the DWI modality, including 3 different 174 stroke types. There were 18 images relative to LACS, 222 175 images relative to PACS, and 27 images relative to TACS. 176 [Fig. 3](#page-5-0) shows an example image for each stroke type. 177

[Table 1](#page-5-0) summarizes the image data details. Column 2 of 178 [Table 1](#page-5-0) details the number of images in the original data- 179 set. There are only 18 LACS images, which is a small series 180 compared to the 222 PACS images. Hence, the initial data- 181 base is imbalanced. To address this problem, we used a 182 synthetic sample method to balance the three considered 183 classes. Column 3 indicates the amount of synthetic data 184 generated for the individual classes. Column 4 states the 185 total number of images, i.e. the sum of original and syn- 186 thetic images. The process of generating synthetic images 187 is described in Sections 2.2–4. 188

2.1.1. ADASYN synthetic sampling 189

In classification and learning methods, it is of funda- 190 mental importance to have a balanced dataset in order to 191 avoid biasness due to disproportionate data distribution. 192 Adaptive synthetic sampling (ADASYN) is employed to 193 boost the performance, by decreasing the bias and balanc- 194 ing the samples ([Haibo, Yang, Garcia, & Shutao, 2008;](#page-10-0) 195 [Molinari, Raghavendra, Gudigar, Meiburger, & Rajendra](#page-10-0) 196 [Acharya, 2018\)](#page-10-0). It is apparent in part 2.1, the initial data-
197 base is very imbalanced, with a high bias toward images 198 with PACS. To overcome this issue, we employed ADA- 199 SYN to balance the database. ADASYN first evaluates 200 the disproportion among different classes, and produces 201 the number of synthetic data for the minority classes there- 202 after, according to the density distribution. The quantity of 203 synthetic samples to be simulated are evaluated by the fol- 204 lowing equation: $(m_1 - m_S) \times \beta$, where β is an empirical 205 parameter between 0 and 1. In this study, we chose $\beta = 1$ 206 to obtain the optimal performance. After ADASYN 207 to obtain the optimal performance. After ADASYN employment, the database then consisted of 223 LACS 208 images, 222 PACS images, and 222 TACS images [\(Table 1\)](#page-5-0), 209 for a total of 667 images. 210

2.2. Automatic stroke detection approach 211

2.2.1. Image preprocessing and Radon transform 212

During the initial processing step, each image underwent 213 adaptive histogram equalization ([Pizer, 1987\)](#page-10-0) in order to 214 enhance the image and increase contrast. The histogram 215 equalization algorithm used local regions within which 216 the contrast is amplified in an adaptive manner. 217

After equalization, the images were processed with the 218 Radon transform (RT) . This projects the pixel values along 219 a radial line at a particular angle onto a two dimensional 220

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Fig. 3. Examples of ischemic strokes and bispectrum images. (A) MRI image of LACS stroke (B) bispectrum image of LACS stroke (C) MRI image of PACS stroke (D) bispectrum image of PACS stroke (E) MRI image of TACS stroke (F) bispectrum image of TACS stroke.

 graph. Algorithmically, the mathematical operation is modeled as a summing the values of pixel in the observed direction [\(Radon, 1986](#page-10-0)). The RT is therefore capable of capturing specific directional signatures from an image, and simultaneously preserving intensity distinctions, to enhance image spatiofrequency information. In this study, 226 we calculated the RT from 0° to 179°, with a step size of 1° . 227

2.2.2. Feature extraction 228

In this step, we extracted features based on Higher 229 Order Spectra (HOS) and various entropies. 230

2.2.2.1. Higher order spectra (HOS). Using the obtained 231 180 1D RT sinogram signals were extracted the higher- 232 order bispectrum entropy and phase features (Nikias $\&$ 233 [Raghuveer, 1987\)](#page-10-0). The bispectrum plots are shown in 234 Fig. 3B, D, F for LACS, PACS and TACS types of stroke 235 respectively. 236

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 Various bispectrum entropies (first, second, third order entropies and phase entropies) were extracted as presented in ([Chua, Chandran, Acharya, & Lim, 2008; Chua,](#page-9-0) [Chandran, Acharya, & Lim, 2008\)](#page-9-0). The bispectrum there- fore is a non-linear method for analyzing images and is able to detect subtle image variation.

 2.2.2.2. Entropy features. Entropy is a measure of uncer- tainty, which is associated with the randomness of the mea- sured structure. In this study, we used seven different measurements of entropy, which are defined here and are explained in more detail in [Singh and Singh \(2010](#page-10-0)):

248 Given that an image $I(x, y)$ has N_i distinct gray levels
249 (where $i = 0, 1, \dots, L_{i-1}$), the normalized histogram from 249 (where $i = 0, 1, \dots, L_{i-1}$), the normalized histogram from 250 a specific region-of-interest (ROI) with dimensions $(A \times B)$ can be defined as: $\frac{251}{252}$

$$
F_i = \frac{N_i}{A \times B} \tag{2}
$$

²⁵⁵ Therefore, Shannon entropy can be expressed as: ²⁵⁶

$$
S_n = -\sum_{i=0}^{L-1} F_i \log_2 F_i \tag{3}
$$

²⁵⁹ Yager entropy can be expressed as: ²⁶⁰

$$
Y = \frac{\sum_{i=0}^{L-1} |2F_i - 1|}{|A \times B|} \tag{4}
$$

²⁶³ Kapur entropy can be expressed as: ²⁶⁴

$$
K_{\alpha,\beta} = \frac{1}{\beta - \alpha} \log_2 \frac{\sum_{i=0}^{L-1} F_i^{\alpha}}{\sum_{i=0}^{L-1} F_i^{\beta}}
$$
(5)

267 where $\alpha \neq \beta, \alpha > 0, \beta > 0$.

271

284

²⁶⁸ Re´nyi entropy can be expressed as: ²⁶⁹

$$
R = \frac{1}{1 - \alpha} \log_2 \sum_{i=0}^{L-1} F_i^{\alpha}
$$
 (6)

272 Vajda entropy is a special case of the Kapur entropy $^{273}_{274}$ where $\beta = 1$, and can be defined as:

$$
V_{\alpha} = \frac{1}{1 - \alpha} \log_2 \frac{\sum_{i=0}^{L-1} F_i^{\alpha}}{\sum_{i=0}^{L-1} F_i}
$$
(7)

²⁷⁷ Fuzzy entropy can be expressed as: ²⁷⁸

280
$$
S_n = -\sum_{i=0}^{L-1} F_i \log_2 F_i
$$
 (8)

²⁸¹ Max entropy can be expressed as: ²⁸²

$$
S_n = -\sum_{i=0}^{L-1} F_i \log_2 F_i
$$
 (9)

285 2.2.3. Feature ranking

286 Feature ranking and the subsequent feature selection 287 plays an important role when building a robust learning 288 model, because these steps will determine which information is presented to the machine classification system. There 289 are various statistical techniques that can be used for select- 290 ing significant features. A particular feature can be consid- 291 ered more important if we can rank the feature among the 292 other features based on some metric. Therefore, a higher 293 ranked feature is more valuable for classification than a 294 lower-ranked feature. Moreover, ignoring features that 295 have a rank lower than a specific threshold can also 296 increase classification speed. 297

In this study, the computed features were ranked using 298 the F-value obtained from analysis of variance (ANOVA) 299 ([Hoaglin & Welsch, 1978\)](#page-10-0). The features with higher F- 300 values are ranked first, and vice-versa. We input the highest 301 ranked features first to the classifiers in the descending 302 order one by one in the descending order until the highest 303 performance is achieved. 304

2.2.4. Classification and validation 305

The following classification methods were utilized in our 306 three-class system: decision tree (DT) , linear discriminant 307 analysis (LDA), quadratic discriminant analysis (QDA), 308 k-nearest neighbor (k-NN), probabilistic neural network 309 (PNN), and support vector machine (SVM) with ten-fold 310 strategy. The SVM classifier (polynomials 1 to 3) and radial 311 basis function (RBF) kernels were used ([Duda, Hart, &](#page-9-0) 312 [Stork, 2012](#page-9-0)). [Acharya et al. \(2016](#page-9-0)) provides a detailed 313 description of each of these classification methods. 314

As discussed in the Introduction, LACS is considered a 315 mild stroke, whereas PACS and TACS are considered as 316 medium and severe strokes, respectively. Therefore, for 317 the calculation of the validation parameters, a LACS is 318 considered as a negative, whereas PACS and TACS are 319 considered as a positive. Hence, the number of true nega- 320 tives correspond to the number of LACS images correctly 321 classified as LACS images, whereas the number of true pos- 322 itives correspond to the number of PACS and TACS 323 images that are correctly classified. 324

3. Results 325

The completely automatic approach presented herein 326 relies first upon image preprocessing, and then on the 327 extraction of specific features, specifically image entropies 328 and higher order spectra entropy and phase features. The 329 final number of features for each image was equal to 79. 330 These features were ranked according to the ANOVA F- 331 value, and the top 45 ranked features are reported in 332 [Table 2](#page-7-0). [Fig. 4](#page-8-0) provides a graphical representation of the 333 feature performance based upon the F-value. As can be 334 observed, the higher order bispectrum entropy and phase 335 features are the highest ranked features, and are therefore 336 the most discriminant for the determination of ischemic 337 stroke with brain MRI imagery. 338

The final results of classification and the number of fea- 339 tures used for each method are reported in [Table 3.](#page-8-0) As can 340 be noted, the SVM with RBF kernel provided the best 341 results, using a total number of 36 features (i.e., the first 342

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Top 45 features sorted using the ANOVA (F-value).

++HOS: higher order spectra; Ent: bispectrum entropy; EntPh: bispectrum phase entropy; the number in subscript corresponds to the order of the bispectrum entropy (i.e., first, second, or third); the number in superscript corresponds to the considered Radon angle.

343 36 listed in Table 2), with an accuracy of 97.6%, a PPV 344 equal to 100%, a sensitivity equal to 96.4%, and a speci-345 ficity equal to 100%.

 Our results demonstrate indicate that, or system is able to correctly identify mild stroke in 100% of cases, and mis- diagnosed a medium or severe stroke as mild in only 2.4% of cases (16 false negatives).

350 4. Discussion

351 It can be seen from the Table 2 that, most of the entropy 352 features gradually decreases from LACS to PACS to TACS. The entropy values decreases depending on the 353 severity of the brain stroke. In LACS, the change in the 354 pixel value is very subtle, so the entropy values are large. 355 In PACS and TACS, there will be more white patches 356 resulting in the reduction of variability in the pixel values 357 and entropy values. 358

Medical imaging technology is progressing toward 359 higher resolution systems, and is capturing more images 360 per patient ([Ng, Faust, Sudarshan, & Chattopadhyay,](#page-10-0) 361 [2015\)](#page-10-0). For example, the field strength in MRI systems is 362 increased to have higher signal-to-noise ratio with a better 363 resolution which is suitable for clinical applications [\(Stucht](#page-10-0) 364

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Fig. 4. Spider diagram to display the F-value for the individual features.

Table 3 Classification results for ischemic stroke identification.

[et al., 2015\)](#page-10-0). That means that human interaction with these 365 images becomes more labor intensive, since the cognitive 366 processes involved in understanding images with more 367 detail requires more time. That extended time requirement 368 is amplified by the fact that there are more images available 369 for analysis. Hence, the goal of decision support systems 370 for reading cardiologists must be to reduce human interac- 371 tion as much as possible. Ideally, a human decision maker 372 should only be presented with suspected positive cases. In 373 our case, the reading radiographer should only see the 374 MRI images that show signs of the selected stroke severity. 375 As a consequence, the automated stroke severity detection 376 systems must have a high sensitivity to reduce the changes 377 of missing true positives, i.e. MRI images showing the signs 378 of the selected stroke severity. State-of-the art decision sup- 379 port systems do not meet these requirements. All of the 380 support systems, as summarized in Table 4, utilize image 381 segmentation techniques that require manual intervention. 382 To be specific, the reading radiographer needs to deter- 383 mine, or at least to confirm, a region of interest within 384 the MRI image. This is undesirable, because of the time 385

++ TP: true positives; TN: true negatives; FP: false positives; FN: false negatives; Acc: accuracy; PPV: positive predictive value; Sens: sensitivity; Spec: specificity.

Table 4

Comparison with rest of the similar works.

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 required to identify the region of interest, and the training required to interact with the decision support system in an optimal way. Furthermore, indicating the region of interest is inevitably associated with problems of inter- and intra- observer variability, which limit diagnostic quality in a practical setting. In the current study, we have undertaken a different approach by using HOS features. Extracting these features does not require manual intervention; hence we established a truly automatic stroke severity evaluation.

 The number of available datasets is crucial for the design of decision support systems, because that dataset limits the amount of transferrable knowledge concerning the disease that can be extracted. In our case, we require the decision support system to function in a practical envi- ronment, where all of the data is unknown, and the stroke severity must be estimated. That estimation is based upon the knowledge extracted from the dataset that was avail- able during the design time. We have used 267 MRI images. These are increased from the number of images N used in prior work [\(Subudhi, Jena, & Sabut, 2018;](#page-10-0) [Subudhi, Acharya, Dash, Jena, & Sabut, 2018](#page-10-0)). Hence, there is the possibility that our system may have improved performance in a practical setting.

 The practical performance of a system cannot be estab- lished during design time. It is only possible to reason about the practical performance based upon statistical measures, such as the accuracy, sensitivity, and specificity. In our study, these measures were established with ten-fold cross validation, which provides a better estimate of the performance achievable for the available dataset. However, we did not attempt a blindfold validation of the system. Neither did any of the studies summarized in [Table 4](#page-8-0) implement a blindfold procedure. This is a shortcoming, because a blindfold validation mimics the use case scenario for the decision support system. The blindfold cases can be established by excluding specific patients from the dataset used for training and testing the classification system. The images from these patients are tested in a separate blindfold validation step. During the design time, we decided against blindfold validation, because it would have restricted the number of available datasets, and hence it would have limited the volume of extractable diagnostic knowledge.

429 5. Conclusion

 In this paper, higher order spectra bispectrum entropy and phase features were used to extract salient information from MRI imagery, for stroke severity estimation. To establish a result, we built an automated decision support system which classifies MRI images as showing signs of PACS LACS or TACS. Through competitive testing, we established that the SVM RBF classifier outperformed DT, LDA, QDA, SVM Poly 1, SVM Poly 2, SVM Poly 3, k-NN and PNN. To be specific, the SVM RBF classifier 439 achieved a sensitivity = 96.4% , specificity = 100% , accu-440 racy 97.6%, and positive predictive value $= 100\%$.

Our decision support system does not require any man- 441 ual intervention from the reading radiographer. Hence, our 442 method is automatic and not affected by inter- and intra- 443 observer variability. We achieved this property by replac- 444 ing features based on image segmentation results with 445 higher order spectra bispectrum entropy and phase fea- 446 tures. Despite that restriction, we were able to achieve a 447 best classification performance among all of the surveyed 448 studies. 449

We have achieved the specificity is 100%. This means 450 that, our proposed system is able to automatically identify 451 all the LACS images correctly. Hence, we will be able to 452 identify the early stage of the brain stroke correctly. 453

Having a truly automatic stroke severity classification 454 support system has the potential to reduce time and effort 455 spent on routine cases. The reading radiographer can there- 456 fore focus on corner cases which require more manual 457 effort to establish an accurate diagnosis. 458

Declaration of Competing Interest 459

The authors declared no conflict of interest in this work. 460

Appendix A. Supplementary material 461

Supplementary data to this article can be found online 462 at [https://doi.org/10.1016/j.cogsys.2019.05.005.](https://doi.org/10.1016/j.cogsys.2019.05.005) 463

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