The work flow of our proposed WMH segmentation method is illustrated in Fig. 1. It consists of two major steps: (1) generate a rough brain mask by training a downgraded U-net fully convolutional neural network (FCN) to segment white matters from T1 images and post-processing using connectivity analysis and morphological operations. This brain mask fulfil the purpose of skull stripping for remove potential false positive WMH outside the brain region. (2) train a U-net [1] like FCN architecture with residual connections to segment WMH by efficient end-to-end training and inference using combined T1 and FLAIR images.



Fig. 1 Overall work flow of proposed WMH segmentation.

Training for the white matter is exactly the same as our previous method, where the training label for the white matter is obtained using the FSL software developed by Oxford. The improvements upon our previous method includes:

(1) We trained the deep FCN using **residual connections over the 2D U-net architecture** instead using downgraded U-net with 3 pooling layers.

(2) The deep FCN is trained by using **multi-spectra MR images** (combined T1 and **FLAIR**), where previously we only use FLAIR images for learning. Also, both T1 and FLAIR images were first normalized to [0, 1] before combined for training and testing.

(3) We improved some training hyper-parameters, such as the global classbalancing weight  $\beta$  and learning rate.

(4) We **modified the post-processing step**: the white matter mask is generated using a higher threshold followed by a morphological dilation operation, instead of a lower threshold. Meanwhile, the post fuzzy-connectivity analysis is removed for WMH segmentation to avoid generating any unexpected false positive.