Deeply Supervised U-Net for Mass Segmentation in Digital Mammograms

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**ABSTRACT**

Mass detection is a critical process in the review of mammograms. The shape and texture of the masses are key indicators in the prognosis of the medical condition. Hence, semantic segmentation is found to be useful in this context rather than mere object detection (or) localization. The main challenges involved in the semantic segmentation of masses in mammograms include (1) higher signal to noise ratio (SNR) (2) indiscernible mass boundaries and (3) more false positives due to significant overlap in the intensities between the normal parenchymal regions and masses. To address these challenges, we propose DS U-Net (Deeply Supervised U-net model) coupled with Dense CRF (Conditional Random Fields). Most of the state-of-art approaches for semantic segmentation uses Encoder - Decoder based model. Encoder captures low-level features such as presence of mass in multiple stages. Decoder path provides the precise segmentation in multiple stages by combining the intermediate results from the encoder at each stage through skip connections. The resulting segmentation map lack the ability of capturing the non-conspicuous and spiculated mass boundaries. In the proposed work, deep supervision is integrated with popular Encoder - Decoder model (U-net) to monitor the low level features for proper attention of the boundaries of suspicious regions and higher level features for accurate segmentation of the entire mass. The final segmentation map is obtained by fusing the intermediate outputs with the final output using learnable weights. The resulting segmentation map is fine tuned using Dense CRF to enhance the edges. We evaluated the model on two publicly available benchmark datasets CBIS-DDSM and INBREAST. DS U-Net with DenseCRF provides Dice score of 84% for CBIS-DDSM and 82.6% for INBREAST.

*Keywords:*

Mass Segmentation, Deep Supervision, Mammograms, Conditional Random Fields

# **INTRODUCTION**

Global Cancer Observatory Database released in 2018 reports that Breast cancer is contributing to over 25.4% of all the new cases diagnosed [1].  Henceforth, Governments are conducting screening programmes to curb the disease. Mammograms are widely adopted as the primary screening tool to diagnose breast cancer. A mammogram is an x-ray image of the breast which captures the changes in the breast tissue. Presence of masses and microcalcifications in the mammogram characterize the disease. The detection of these regions in mammograms are difficult as their pixel intensities often correlate with normal tissue.

CAD (computer aided detection) tools uses digitally captured images of the mammogram and employs artificial intelligence based techniques to detect suspicious regions in them. CAD has been constantly evolving with the advent of new techniques in the domain to provide accurate results. With the recent success of deep neural networks in most of the vision oriented challenges, they are been explored for medical diagnosis.

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| **INBREAST Database** | | **CBIS-DDSM Database** | |
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**Fig 1: Examples of Mass segmentation First row: Full Field of View Mammogram Images in INBREAST and CBIS-DDSM dataset, Second row: Manually segmented mass regions**

The main contributions of the work include:

1. We propose Deep Supervised U-net for mass segmentation in whole mammograms to monitor the attention of the intermediate layers.  Encoder layers are directed towards proper attention of the mass boundaries and decoder layers are directed towards proper attention of the mass regions. This reduces false positives and leads to faster convergence.
2. We use a learnable fusion layer to fuse the output of the attention layers with the last layer to produce the final segmentation result.
3. We employ Combined loss function for the fusion layer to address the class imbalance problems (mass usually occupies a smaller percentage of the entire image). This loss penalizes the false positives more.
4. Unlike other works, we use preprocessing and post processing steps to improve the accuracy of the model. CLAHE is used to enhance the contrast of the input mammogram images and Dense CRF is used to recover the mass boundaries which got smoother due to the rigorous downsampling.

# **Method**

## **Overview**

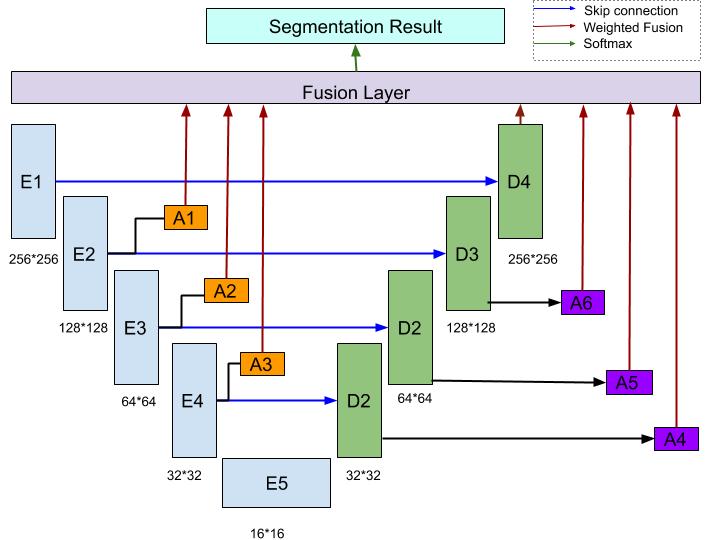
The proposed model employs an end-to-end framework for mass segmentation in mammograms.  The input images are processed through Contrast limited Adaptive histogram equalization technique (CLAHE).  The resulting images are then normalized and resized to 256\*256 to train Deep Supervised U-net. During the testing phase, resulting softmax probabilities of DS U-net are further refined using Dense CRF for  definite edges. Fig 2 shows the various components involved in the proposed work.

## **Preprocessing**

Preprocessing is often neglected when deep neural networks are used for segmentation. But, mammogram images exhibit high SNR and hence the detection becomes infeasible without proper preprocessing. Histogram equalization and its variants are found to be efficient for mammogram images[10][11]. Hence, CLAHE has been adopted to improve the local contrast of the image. The algorithm is also found to improve the edge boundaries in each region of the image. Fig 3 shows the sample images from INBREAST and CBIS-DDSM which are enhanced using CLAHE.

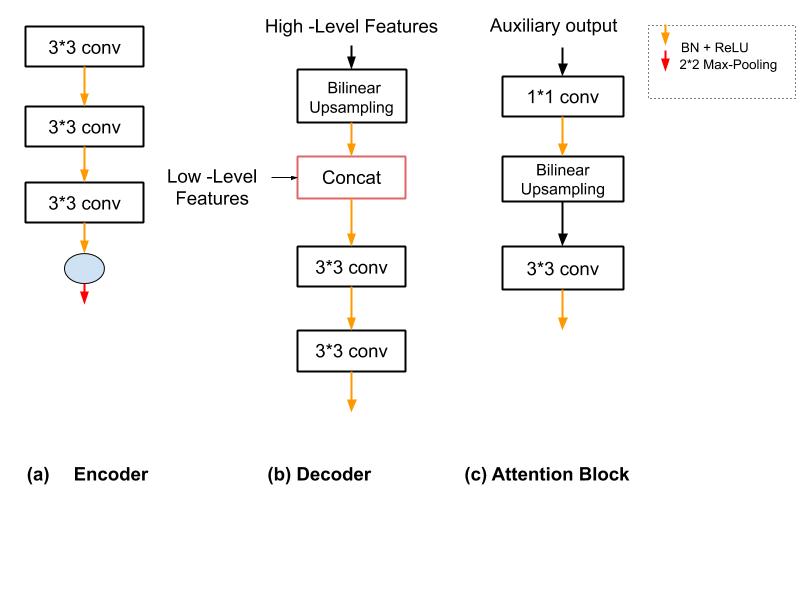
## **Deep Supervised U-net**

Deep Supervised nets [6][7] brings in transparency to the intermediate hidden layers in deep neural networks by considering their error factor with respect to the ground truth in the training objective criterion. It has improved robustness of the neural networks in both segmentation and classification[6]. In segmentation, the output of intermediate layers are upsampled and compared with ground truth to quantize their error margin.  U-net[9] has become the de-facto standard for biomedical image segmentation. It employs an encoder decoder based architecture. Encoder consists of convolution layers for retrieving contextual information and pooling layers to downsample the images. Downsampling facilitates retrieval of higher level contextual information. Unet has symmetrical decoder path which upsamples the information to get the spatial context of the retrieved information. Skip connections are pathways which carry the spatial information from encoder to decoder pathway. Many works have further improved U-net by varying upsampling techniques , using mixed pooling techniques (or) modifying the loss functions. Due to the symmetricity of the encoder and decoder , Unet always produces smoother segmentation map. Hence, DS U-net is used to obtain finer boundaries and eliminate the false positives. The proposed work has extended over the idea of Chen et al[8] and Mishra et al[9] to use different intermediate layers of segmentation network to focus on the boundaries and regions simultaneously. Fig 4 shows the complete architecture of the DS U-net.

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**Fig 4: Complete architecture of the Deeply Supervised U-net. Auxiliary layers A1,A2 and A3 are providing attention to the boundaries and Auxiliary layers A4, A5 and A6 are used to discriminate the entire mass region from the background**

The encoder block applies repeated 3\*3 convolution on the input tensor as shown in Fig 5(a). The Decoder block (Fig 5(b))up-samples the high level features from the previous layer using bilinear interpolation and  combines it with spatial context (low level features) from the encoder blocks. Subsequently, 3\*3 convolution is applied before passing the tensor to the next layer. Blocks A1 - A6 are attention blocks which supervises the respective encoder and decoder layers as shown in Fig 4. It applies 1\*1 convolution to reduce the  dimensions and bilinear upsampling to enlarge the intermediate tensor to match the output dimension. Finally, a 3\*3 convolution is applied to obtain the activations of the intermediate layers. Fusion layer weighs the outputs of attention blocks and final decoding layer(D4) to produce the end segmentation result as shown in eq(1).

**Fig 5: Various blocks of the DS U-net architecture**

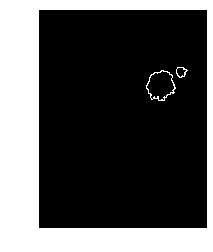
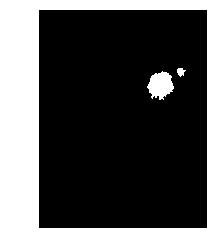
(1)

Here, represents the final segmentation result, O(.) represents the softmax activations of the respective layers and {} represents weights associated with output of final decoder block and attention blocks respectively.The objective criterion is modified as in eq(3) so that attention blocks A1 - A3 steer the network towards proper boundary identification and blocks A4-A6 steer the network towards region identification.

(2)

Where L represents Combined loss function which is discussed in section D, represents the parameters of the network which includes (Wencoder,Wdecoder, Wattention,h), YB represents the ground truth which includes only the boundary pixels of the suspicious masses and YMthe ground truth which includes the region of the suspicious masses.  A factor of

is used to reduce the impact of attention layers when the number of iterations (t) approach the total number of epochs[7].  The mask for boundary is obtained by performing erosion on the region mask with disk shaped structuring element (value of radius is set to 20) and subtracting the resultant from the original image. The boundary mask obtained after the morphological operation is shown in Fig 6.



(a)

(b)

**Fig 6: Segmentation masks : (a) Region Mask (b) Boundary Mask**

## **Loss Function**

To address the class imbalance problem two metrics: Sorensen Dice Score(DS) and Cross Entropy Loss(CEL) are used to gauge the differences between the prediction and the ground truth [12][13]. Combined loss function is used as it is reported that the network gets unstable when a single metric is used[12]. Consider represents the ground truth of pixel which belongs to [0,1] where 0 represents the background (normal region) and 1 represents the mass (abnormal region) and pirepresents the softmax probabilities of the predicted segmentation.  Binary CEL between predictions and targets are described in eq(3)

(3)

The value is summed over all pixels in an image . The value of cross entropy loss lies between 0 and 1. 0 indicates perfect segmentation and 1 represents the vice versa. Sorensen Dice score is described in equation (4):

(4)

is known as the smoothing factor which is set to default value of 1e-5 throughout the experiment.The combined Loss function L is given as

= (5)

## **Post-Processing**

Though DS U-Net offers precise segmentation of the objects, the resulting segmentation map yields smoother boundaries losing the vital information in the process. Probabilistic graphical models have proven to be effective in modeling the neighborhood dependencies thereby possess higher discriminatory power to differentiate the foreground from the background. Hence, Conditional Random Fields are used to fine-tune the resulting segmentation map of Deep Supervised U-Net model. Works by Chen et al[2] and Zheng et al[3] showed that state of the art segmentation results can be obtained by incorporating the DenseCRF model. The model accepts the raw intensity values of input image and the unary potentials to generate the final probability map as shown in Fig 7.

CRF model treats the individual pixels as random variables which can take values from the set where 0 indicates background and 1 indicates foreground (suspicious mass region). CRF inference assigns a configuration for every random variable in the image such that the energy given in equation (6) is minimized given the original pixel intensities of an image .

(6)

The term denotes the unary cost associated with assigning label x for the variable. This cost is usually obtained from the classifier. The interdependencies between pixels are modeled using pairwise cost which accounts for cost involved in assigning labels x and y for the pixels and respectively. The common pairwise cost used is potts model which provides a cost of 0 when the neighboring pixels are assigned with same label and a value of 1. Finding such a configuration is an NP-hard problem. Further, certain assumptions should also be made on how the pixels connect with each other. There are two popular configurations used: Grid CRF and fully connected CRF. Fully connected CRF assumes that every pixel in the image is connected to every other pixel where Grid CRF assumes that the pixel is connected only to its adjacent pixels. Dense CRF leverages on fully connected CRF to model the neighborhood dependencies. CRF has been formulated on the basis of the gibbs distribution as given in eq(7).

(7)

The learning phase of CRF is defined as computation of marginal probabilities for every random variable and for every pair of random variables (, ) which are connected by edges (i.e) all pixels except itself in a fully connected graph. Once the marginal probabilities are computed, inference phase chooses the configuration which maximizes the joint probability. Detection of true distribution for the unary and pairwise potentials are infeasible. Mean Field Inference approximates the p(X|I) by considering a simpler distribution Q(X|I) and iteratively reducing the Kullback Leibler divergence between Q(X|I) and p(X|I) using pixel intensities of the original image. Unary potentials are obtained from the deep neural networks and the pairwise potentials are modeled using sum of two gaussian kernels as suggested in [4]: Gaussian smoothing kernel and Gaussian preserved bilateral filtering kernel. Here, and denotes the positions of the pixels and and denotes the intensity of the pixels. Weights are associated with the kernels to control the significance of the filters as per the demands of application. Thus, the pairwise potentials in CRF is formulated aswhere denotes the label similarity using common potts model and k denotes the sum of gaussian kernels. Mean Field updates are provided as in eq (8).

= (8)

Here , indicate the strength of the filter m. In our experiments, we have used a value of 0.75 for gaussian filter and 0.25 for the bilateral filter.The algorithm for computation of final probabilities based on Mean Field Inference is as follows:

|  |
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| **Algorithm 1: Mean Field Inference for Dense CRF** |
| **Input :**  I Input grayscale Image  Output of last decoding layer of DS U-net  **Output:**  Probabilities of various labels of the pixel computed using CRF |
| **Initialize** parameters  - a vector of size 1 x m - vector of size m x m where m denotes the number of filter kernels |
| **Initialize**  with the softmax on unary potentials |
| **while** T< ( denotes the number of iterations) |
| = 0 |
| For every filter in the set {gaussian smoothing filter, gaussian bilateral filter} |
| += w[i] \* sum of filtering coefficients of all other pixels based on Input Image () |
| = where represents matrix of values computed for all possible labels (l’) |
| = -- |
| = Compute softmax over considering pixel value of all the other labels |
| **end while** |

# **Experiment**

## **Datasets**

The model was evaluated on two popularly available benchmark datasets: INbreast[14] and CBIS-DDSM[15]. INbreast contains 107 Full Field Digital Mammography (FFDM) images with mass findings. The images are available in DICOM format and size of the images is either 3328 \* 4084 (or) 2560 \* 3328 with 14-bit resolution. The boundary pixels of suspicious masses are manually annotated and available in XML format. Because of its small size, we performed a three fold cross-validation on the dataset to gauge the model’s performance.

CBIS-DDSM dataset contains curated mammogram images from DDSM, a largest available mammogram database. They provide separate training and test set for mass detection and microcalcification detection. The dataset comprises of FFDM images along with the segmentation mask and cropped ROI for every suspicious finding in DICOM format. Mass detection dataset contains 1381 images for training and 378 images for testing. Multiple ROI detected in an image are provided as separate images. In our experiments we merged the multiple masks of an image into a single mask before training which resulted in 1231 training images and 361 testing images. The entire dataset has been used for the evaluation of the proposed method. Both the datasets has significant amount of benign cases [13] and it also includes masses of varying sizes as shown in Fig 1.

## **Experimental framework**

All the experiments are carried out on NVIDIA GTX 1080 Ti using Tensorflow. The models are trained using mini-batch SGD with batch size of 20 images. AMSGrad[16] is used for optimization and piecewise learning rate policy is adopted to change the learning rate across different invocation of optimizer function. We use learning rates as [1e-4, 5e-3, 3e-2] at the start of epochs [0,150,200] respectively. The learning rates are identified by conducting line search for varying log scales extensively. The models are trained for about 500 epochs. All the learnable weights are randomly initialized as other initializers fail to converge. No data augmentation is used in the experiments.

## **Metrics**

The models are evaluated based on two criteria : object level and pixel level. The widely used object level criteria is F1 score which is defined as:

(9)

Where precision and recall are inversely proportional to each other. Both the measures estimate the accurate detection of masses. Precision is defined as and recall is defined as . They are computed at the image level where measures the number of positive detections (regions) that overlap with the ground truth ,counts the number of false activations and accounts for the missed mass detections. False negatives are created due to under-segmentation which happens when the mass occupies very small regions and share very similar intensity with the normal regions. False positives are the consequence of over-segmentation where the normal parenchymal regions are detected as masses.

To further account for exact boundary extraction, two pixel level measures are used. One is the sensitivity which measures the exact amount of overlap between two detected mass regions which is defined as

(10)

Here, TP measures exact count of mass pixels which are classified correctly whereas counts the number of mass regions. Similarly , FP denotes the count of normal pixels classified as mass. The next measure dice similarity coefficient is given by

(11)

This measure is a tradeoff between over segmentation and under segmentation.

## **Experimental Results**

1. **TABLE I: Evaluation metric values observed from the outputs of different approaches for whole mammograms**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Dataset/**  **Network** | **INBREAST** | | | **CBIS - DDSM** | | |
| **F1 Score** | **Sensitivity** | **Dice Index** | **F1 Score** | **Sensitivity** | **Dice Index** |
| U-net | 71.87 | 87.35 | 64.91 | 65.2 | 88.32 | 70.08 |
| DS U-net (B) | 74.35 | 86.45 | 69.102 | 69.76 | 89.41 | 75.65 |
| DS U-net (R) | 75.01 | 87.17 | 74.82 | 72.4 | 86.9 | 78.46 |
| DS U-net | 79.19 | 85.22 | 76 | 79.13 | 87.11 | 76.5 |
| DS U-net + Dense CRF | 80.5 | 87.8 | 81.72 | 82.89 | 88.34 | 82.01 |

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Be aware of the different meanings of the homophones “affect” (usually a verb) and “effect” (usually a noun), “complement” and “compliment,” “discreet” and “discrete,” “principal” (e.g., “principal investigator”) and “principle” (e.g., “principle of measurement”). Do not confuse “imply” and “infer.”

Prefixes such as “non,” “sub,” “micro,” “multi,” and “ultra” are not independent words; they should be joined to the words they modify, usually without a hyphen. There is no period after the “et” in the Latin abbreviation “*et al.*” (it is also italicized). The abbreviation “i.e.,” means “that is,” and the abbreviation “e.g.,” means “for example” (these abbreviations are not italicized).

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# **Conclusion**

A conclusion section is not required. Although a conclusion may review the main points of the paper, do not replicate the abstract as the conclusion. A conclusion might elaborate on the importance of the work or suggest applications and extensions.

**Appendix**

Appendixes, if needed, appear before the acknowledgment.

**Acknowledgment**

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