Image Segmentation of Nucleus Breast Cancer using Digital Image Processing

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Abstract: One of examination methods of breast cancer cells is using Immunohistochemistry (IHC). IHC is used to determine the status of Estrogen Receptor (ER) and/or Progesterone Receptor (PR). The bonding reaction occurring between the cell and the painting results in the color of the nucleus cell being blue which signifies the negative and brown ER/PR hormone for positive ER/PR. The given hormonal therapy will be effective to breast cancer patients if they have positive ER/PR receptors. Up to now the Anatomy Pathology specialist calculatses the percentage of positive cells that have been marked semiquantitatively. This is time-consuming, costly, subjective and tedious, thereby impacting the length of time required in determining appropriate therapy for breast cancer patients. This study analyze the image of IHC breast cancer to determine the assessment of ER/PR hormone receptor using image processing. The use of kernels of different sizes shows differences in the results of cell segmentation in connective tissue. The use of 3×3 and 1×1 kernels has indeed succeeded in removing cells in the connective tissue, but not all cells in the connective tissue can be identified. If this step has been completed, then the next process until cell count can be done.

1 INTRODUCTION

Breast cancer is a dangerous disease that occurs due to the uncontrolled cells growth. One of examination methods of breast cancer cells is using Immunohisto-chemistry (IHC). IHC is used to determine the status of Estrogen Receptor (ER) and/or Progesterone Receptor (PR). The IHC technique is performed by applying Hematoxylin and Diaminobenzidine and observing the antibody presence bonds by microscope based on the observation by Pathologyst. The bonding reaction occurring between the cell and the painting results in the color of the nucleus cell being blue which signifies the negative and brown ER/PR hormone for positive ER/PR. The given hormonal therapy will be effective to breast cancer patients if they have positive ER/PR receptors. IHC image Positive estrogen receptors and negative show in the Figure 1.

Up to now the Anatomy Pathology specialist calculatses the percentage of positive cells that have been marked semiquantitatively. This is time-consuming, costly, subjective and tedious (Limsiroratana and Boonyaphiphat, 2009; Estrogen,), thereby impacting the length of time required in determining appropriate therapy for breast cancer patients. This study will an-
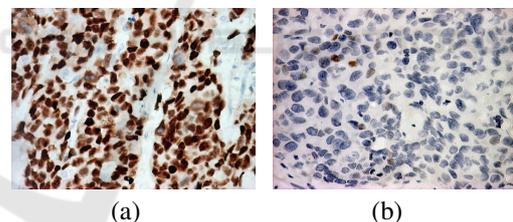

Figure 1: IHC image (a) Positive estrogen receptors (b) Negative estrogen receptors

alyze the image of IHC breast cancer to determine the assessment of ER / PR hormone receptor using digital image processing which is expected to help doctors to determine whether the breast cancer patients require hormonal therapy or not.

(Kostopoulos et al., 2007; Calhoun et al., 2019) provides a positive estrogen receptor assessment by analyzing IHC images using a color texture feature. Assessment of positive ER receptor status with computer method is done through 2 stages, ie. stage I of segmentation of nucleus using Otsu's global image threshold method and morphology operation and stage II classification of nucleus based on brown and blue color using feature selection and K-Nearest

Neighbors weighted voted (KNN-WV).

(Yulianti et al., 2014; Akbari et al., 2011) segmented the immunohistochemical image of estrogen receptor to breast cancer using watershed marker. (Labellapansa et al., 2016) conducted a similar study but using the IHC HER2 method for scores of 1+ and 3+ and the classification can be done correctly 100% for scores of 3+ and 65% for scores of 1+.

This study was able to indicate the status of ER / PR and remove the stacked cell area however the connective tissue cell that is not a nucleus cell counts as ER / PR cell as shown in Figure 2. Our research will make image improvements by removing connective tissue that is not a nucleus cell which hopefully will be able to calculate the number of ER / PR cells in more detail.
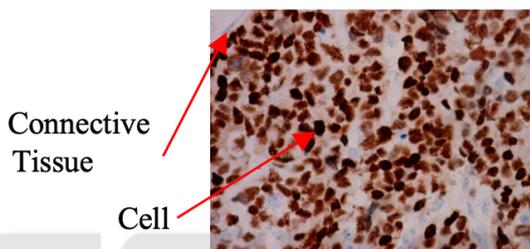
Connective Tissue

Cell

Figure 2: IHC image positive estrogen receptors

2 RESEARCH METHOD

The first step is done by acquiring positive / negative images of ER / PR in the lab Medicine Faculty of Gajah Mada University. The phases of pre processing the imagery are done by using the median filtering method. The clean image of the noise, will enter the segmentation stage to separate the blue area (negative cell ER / PR) and brown area (positive cell ER / PR) using colour deconvolution. The Color deconvolution method can read the colors of each channel Red Green Blue (RGB)(Ruifrok et al., 2001). Watershed is used to separate the stacked cell area using color deconvolution. The next step which is the most important contribution in this study is to identify the connective tissue that is not a cell. The shape feature will be used to remove this connective tissue area. The next step is to calculate the portion of positive cell and negative cell so that can be identified whether the image is positive ER / PR or negative. Flow Chart of Research Activities as shown in Figure 3.
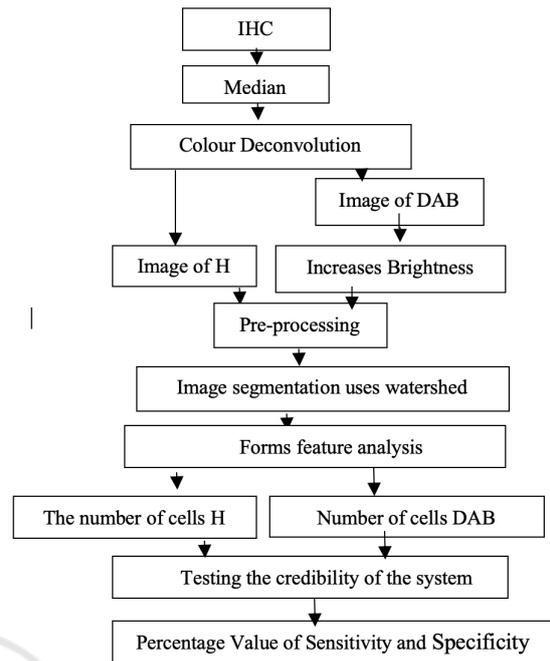
Figure 3: Flow Chart of Research Activities

3 RESULT AND DISCUSSION

The phases of nucleus IHC breast cancer image segmentation are shown in Figure 4. The input image (a) is pre-processed using the median filter (b) then color segmentation is done using color deconvolution so that the image of channel 1 H (c) and channel 2 DAB Positive (d) The next step is to separate the accumulated cells in the H image and the positive DAB image by using watershed marker segmentation. Figures 4 (e) and (f) are the results of the segmentation so that it is expected that the number of cells can be calculated.

Morphological reconstruction was carried out after the process in Figure 4 was completed. Morphological reconstruction is a morphological transformation involving two images and one structural element. The first image is the start point of transformation, commonly referred to as the marker and the second image as a constraint, commonly referred to as a mask. The process of morphological transformation is based on the concept of pixel neighbors using structural elements (Gonzalez et al., 2002). Pixel neighbor operation is an image processing operation to get the value of a pixel that involves neighboring pixel values and is mostly used for form analysis (Kadir, 2017).

The use of kernels of different sizes shows differences in the results of cell segmentation in connective tissue. This study uses a kernel size of 3x3 and 1x1.
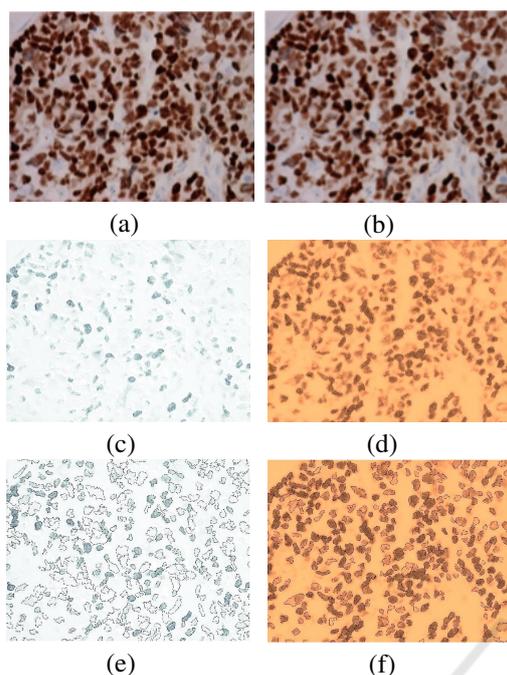
Figure 4: The Stage of IHC Nucleus Image Segmentation Stage of Breast Cancer (a) Image of estrogen receptor (b) Image Resulted by Median filtering (c) Image H Resulted by colour Deconvolution (d) Image DAB Resulted by Colour Deconvolution (e) Image H Resulted by Watershed (f) Image DAB Resulted by Watershed
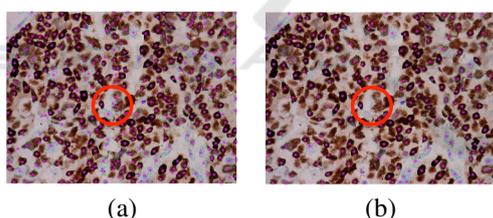

Figure 5: Image of the result of using (a) 3x3 Kernel Size (b) 1x1 kernel size

Figure 5 is the result of cell segmentation in connective tissue using a 3x3 and 1x1 disk kernel. It is seen that cells in the connective tissue are still counted as many cancer cells while using a 1x1-sized kernel seen in cells in the connective tissue there are not many counts.

Based on the results seen in figure 5, the use of 3x3 and 1x1 kernels has indeed succeeded in removing cells in the connective tissue, but not all cells in the connective tissue can be identified. This research will be continued by using other methods to remove cells in connective tissue. If this step has been completed, then the next process until cell count can be done.

4 CONCLUSIONS

From the steps that have been done above, some results are obtained, namely stages of digital image processing to read IHC breast cancer images to obtain H cell counts and positive DAB cell numbers beginning with the pre-processing process using Median Filtering, then proceed with colour segmentation using Colour Deconvolution to obtain IHC H images and positive DAB IHC images and followed by cell segmentation using Watershed Markers. The use of 3x3 and 1x1 kernels has indeed succeeded in removing cells in the connective tissue, but not all cells in the connective tissue can be identified. This research will be continued by using other methods to remove cells in connective tissue. If this step has been completed, then the next process until cell count can be done.

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REFERENCES

Akbari, H., Uto, K., Kosugi, Y., Kojima, K., and Tanaka, N. (2011). Cancer detection using infrared hyperspectral imaging. *Cancer science*, 102(4):852–857.

Calhoun, M. E., Chowdhury, S., and Goldberg, I. (2019). Medical analytics system. US Patent 10,255,997.

Estrogen, S. C. I. R. Kanker payudara menggunakan marker watershed.

Gonzalez, R. C., Woods, R. E., et al. (2002). Digital image processing.

Kadir, A. (2017). Teori dan aplikasi pengolahan citra.

Kostopoulos, S., Cavouras, D., Daskalakis, A., Bougioukos, P., Georgiadis, P., Kagadis, G. C., Kalatzis, I., Ravazoula, P., and Nikiforidis, G. (2007). Colour-texture based image analysis method for assessing the hormone receptors status in breast tissue sections. In *2007 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pages 4985–4988. IEEE.

Labellapansa, A., Muhimmah, I., and Indrayanti (2016). Segmentation of breast cancer cells positive 1+ and 3+ immunohistochemistry. In *AIP Conference Proceedings*, volume 1718, page 110002. AIP Publishing.

Limsiroratana, S. and Boonyaphiphat, P. (2009). Computer-aided system for microscopic images: application to breast cancer nuclei counting. *INTERNATIONAL JOURNAL OF APPLIED*, 2(1):69.

Ruifrok, A. C., Johnston, D. A., et al. (2001). Quantification of histochemical staining by color deconvolution. *Analytical and quantitative cytology and histology*, 23(4):291–299.

Yulianti, A., Muhimmah, I., and Indrayanti, I. (2014). Segmentasi Citra Imunohistokimia Reseptor Estrogen Kanker Payudara menggunakan Marker Watershed. *Seminar Nasional Informatika Medis (SNIMed)*, 0(5):1–10.