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Medical image classification in breast sentinel lymph node detection

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Abstract

With the advent of computational imaging technologies, machine learning now provides an essential supporting modeling tool for disease detection. Breast Sentinel Lymph Node detection requires medical image classification from Raman spectral image dataset. This is achieved with a convolutional neural network, a machine learning technique.

The current efforts on this literature review aim to explore a branch of deep- learning for the detection of first breast cancerous lymph node from Raman Spectroscopy Probe. With this technique, we evaluate the use of a convolutional neural network, a type of machine learning- based algorithm, used to automatically detect cancer metastases in lymph nodes with high accuracy from trained Raman Spectral Dataset.

Keyword: Machine learning; Convolutional Neural Network; Breast Sentinel Lymph Node; Raman Spectroscopy

1. Introduction

Sentinel Lymph Node is the first node (s) to which cancer cells drain directly from a primary tumor. The most common way to assess regional lymph node status is through the sentinel lymph node procedure known as sentinel lymph node biopsy. Besides, the first step in determining the presence of metastases is to examine the regional lymph nodes. Not only is the presence of metastases in these lymph nodes a poor prognostic factor by itself, but it is also an important predictive factor for the presence of distant metastases (Voogd et al, 2001).

2. Raman Spectroscopy Probe for Breast Sentinel Lymph Node

Pathologists examine a glass slide containing a tissue Section of the lymph node stained with hematoxylin and eosin (Geert et al, 2018).

On the other hand, Raman Spectroscopy is noninvasive and has high specificity. Thus, its clinical application is very promising. Furthermore, Raman Spectroscopy has provided free staining techniques (without dye) lately. It can distinguish malignant tissues from noncancerous/normal tissues and can assess tumor margins or sentinel lymph nodes during an operation. Raman images reveal an inhomogeneous distribution of different compounds, especially proteins, lipids, micro calcifications, and their metabolic products, in cancerous breast tissues. Nowadays, studies focus on using Raman spectroscopy to differentiate between benign and malignant tissues in place of traditional biopsy (Saha et al ,2012). Raman spectroscopy can provide real time information, making its intraoperative use possible. Monitoring sentinel lymph node and surgical margins for breast-conserving surgery using Raman spectra can shorten the operative time. Smith et al. used mapping Raman spectra to accurately Judge lymph node metastases (Smith et al, 2003).

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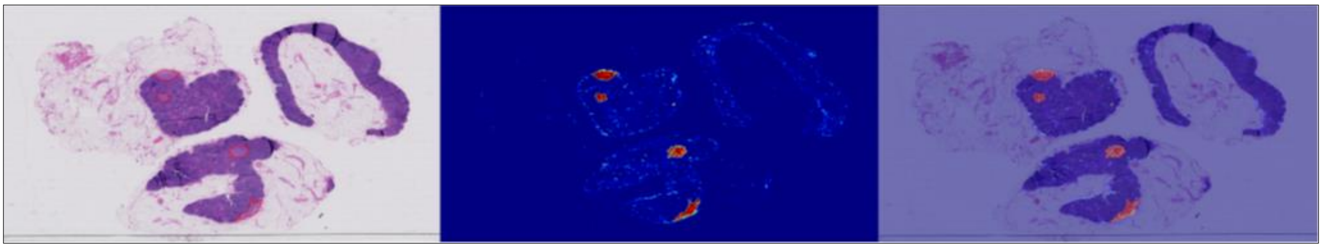
3. Breast Sentinel Lymph Node Detection

In breast cancer, the most common way to assess the regional lymph node status is the sentinel lymph node procedure. With this procedure, a blue dye and/or radioactive tracer is injected near the tumor. The first lymph node reached by the injected substance, the sentinel node, is most likely to contain the metastasized cancer cells and is excised, histopathologically processed, and examined by a pathologist (Giuliano et al, 2011). This tedious examination process is time-consuming and can lead to small metastases being missed (van Diest, 2010). However, recent advances in whole-slide imaging and machine learning have opened an avenue for analysis of digitized lymph node sections with computer algorithms (Geert et al, 2018). For example, convolutional neural networks, a type of machine-learning based algorithm, can be used to automatically detect cancer metastases in lymph nodes with high accuracy from Raman Spectroscopy probe. This is the aim of the review.



(a) Tumor Slide (b) Heat map (c) Heat map superimposed on slide

Figure 1 Visualization of tumor region detection

4. Image Analysis

To start with, the diagnosis of a disease or getting its grading in histopathology images deals with identification of histological structures like cancer cell nuclei, glands, lobule formation as in case of breast cancer. The morphological appearance of these structures like size, color intensity and shape are also important factors for detecting the presence of disease. To analyze all these indicators histopathology images firstly should be segmented (A D Belsare and M M Mushriff , 2012).

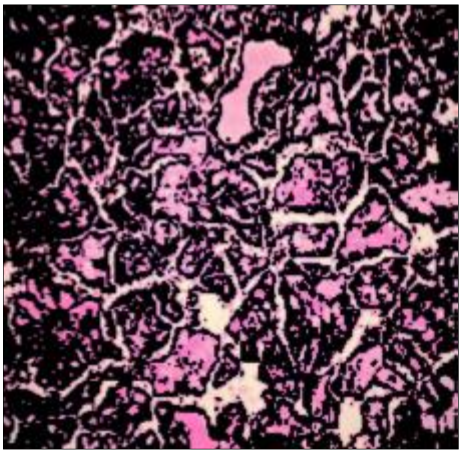


Figure 2 Segmented Image

Due to the complex nature of Pathological images, standard segmentation methods or modified versions of them like Thresholding, Hidden Markov model is used in Rajpoot et al. and Sertel et al. paper of image analysis. Different type of features is extracted from histopathological images for the detection and diagnosis of cancer. Young et al extracted pixel level features for the detection of cancer. These features provide the lowest level of information hierarchy (Kothari et al, 2009). Color features describes about image prominence, color spread and so on. Texture features describe image sharpness, contrast and changes in intensity values. Shape based features provide information about contour and region based features. Contour based features include properties of shape boundary such as Perimeter, bending energy etc. Region based features include area, side length and so on.

5. Batch Effects

Although researchers have developed computer aided systems in diagnosing cancer by extracting different features from histopathological images , when these histopathological pictures are captured from different experimental setups, its prediction performance may decrease due to non-biological experimental variations such as age of sample, method of slide preparation, laboratory, technician, and atmospheric ozone level. Invariably it leads to Batch Effects. Batch effects may lead to huge dissimilarities in features extracted from images. Therefore, it is difficult to identify patients using prediction models accurately.

6. Batch Effects Removal

Normalization methods are applied to remove batch effects occurring in histopathological images. Different types of batch effect removal methods are standardization, mean centering and ratio based method.

Standardization normalizes the standard deviation of all features across samples within each batch to unity. After performing transformation, each feature may have zero-mean across all samples within each batch. In mean centering, the mean of each feature across all the samples within each batch is set to zero. This approach is also known as zero-mean or one-way analysis of variance adjustment. Most of the batch effect removal methods can reduce this variance to almost nearly zero, but combat normalization performance is the best. Then medical image classification can be performed for the dataset of the sentinel lymph node.

7. Medical Image Classification

Medical Image classification is defined as a process of finding model from a database of image features which predict unknown class label, according to medical image techniques (Hiral Kotadiya et al, 2018).

There are seven most commonly used classification algorithms along with the python code: Logistic Regression, Naïve Bayes, Stochastic Gradient Descent, K-Nearest Neighbors, Decision Tree, Random Forest, and Support Vector Machine (Rohit Garg, 2018).

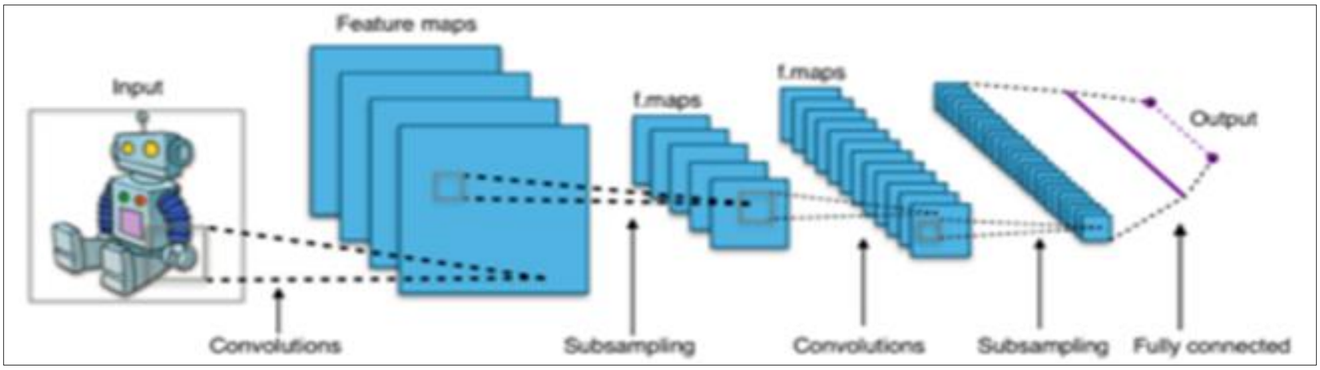


Figure 3 A Typical Convolutional Neural Network Architecture

Machine learning techniques often used in digital pathology image analysis are divided into supervised learning and unsupervised learning (Daisuike and Shumpei, 2017). The goal of supervised learning is to infer a function that can map the input images to their appropriate labels (for example cancer) well using training data (Daisuke and Shumpei, 2018). Labels are associated with a Whole Slide Image or an object in Whole Slide Image. On the other hand, the goal of unsupervised learning is to infer a function that can describe hidden structures from unlabeled images (Daisuke and Shumpei, 2018).

Besides, from the research work of Michael et al 2017 convolutional neural network (CNN) or deep representation feature using pre-trained Convolutional Neural Network has achieved great success in general image analysis, many research applies CNN to pathological images.

Classification is the activity in which objects, concepts, and relationships are assigned to categories. We cannot think about the world unless we order it into categories and categories also help us to act upon the world (Ellen, 1996, p. 155).

However, despite advances in the diagnosis of breast cancer, some limitations remain:

- Neither ultrasound nor mammography can make a qualitative diagnosis, so invasive biopsy or even surgery remains the gold standard in breast cancer.
- Sentinel lymph nodes in intraoperative frozen sections cannot identify the metastasis of the lymph node with 100% accuracy.
- Examinations such as pathology in current clinical application cannot provide information at the molecular or cellular level.

Considering its real-time nature without the need for preparation, Raman spectroscopy is a promising new technique in intraoperative margin assessment and Sentinel Lymph Node Biopy.

More importantly, it is necessary to construct a mathematical model using Raman spectrum data that are obtained from normal and malignant tissues based on various biochemical characteristics such as calcification, protein structure, and fat structure, Pin Gao et al 2o17.

From the foregoing discussions, it could be established that convolutional neural network based machine learning algorithm has not been reported for Breast Sentinel Lymph Node detection using Raman spectroscopy. It also suggests the need to train Raman spectral dataset using supervised and unsupervised (cluster method) machine learning of Convolution Neural Network for medical image classification (Subrata ,2019).

Future Perspective

Breast Sentinel Lymph Node Detection will advance in real-time with Raman Spectral Mapping, especially with Surface Enhanced Raman Spectroscopy Probe. A recent study evaluated the use of novel technology, gold-silica surface-enhanced resonance Raman spectroscopy (SERRS), reporting promising results with the use of nanoparticles. Another exciting research avenue will be the development of new data fusion algorithms for combining radiologic, histological, and molecular measurements for improved disease characterization.

8. Conclusion

Machine learning has greatly enhanced the early detection of cancers, most especially metastatic breast cancer. It holds great promise for the reduction of morbidity rate of the second leading cause of death among women worldwide. The routine use of Sentinel Lymph Node biopsy could significantly decrease surgery-related morbidity, without jeopardizing oncological outcome. With the introduction of routine Sentinel Lymph Node biopsy for the surgical treatment of other malignancies, improvement in patient quality of life is expected. More studies are needed to test the use of new agents and computational imaging technologies in conjunction with Sentinel Lymph Node biopsies.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

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