

Visual Computing Models in Cancer: PET/CT, CAD, CNN, and ST-Net

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ABSTRACT

Visual computing is a discipline in computer science that allows computers to acquire, process, and analyze visual data. In the application field of medicine, it enables the development of new methods for the visualization, detection, and analysis of diseases. Therefore, it plays a significant role in developing the understanding of diseases. Taking the fact that cancer is currently one of the deadliest and most frequent diseases around the world into consideration, it is crucial to generate effective methods for the study of cancer in order to provide appropriate management strategies for the disease and treatment methods. Research has shown that methods based on visual computing can detect, classify, and analyze the cancerous tissues in a patient successfully with high accuracy. This paper focuses on the PET/CT, CAD, CNN, and ST-Net visual computing models by evaluating their working mechanisms, their efficacy in the use of cancer with the help of previous research made in the literature, and their limitations in a medical approach.

Introduction

Cancer, a disease occurring as a result of uncontrolled cell division and metastasis, stands out as a serious medical phenomenon due to the high rates of death and incidence around the world. According to the data provided by the World Health Organization, cancer cases have been rising rapidly over the years. Therefore, cancer has been known as a crucial threat in medicine. However, studies have shown that methods for visual computing can provide successful results for the detection and classification of cancer with high accuracy, indicating that visual computing has a promising future for cancer research.

Visual computing includes computed tomography (CT) and nuclear medicine scans (bone scans, PET scans, thyroid scans, MUGA scans, and gallium scans), computer-aided detection (CAD), x-rays, convolutional neural network (CNN), magnetic resonance image (MRI), ST-Net algorithm, and VGGNet model, which shows that visual computing is used in the study of cancer in a wide range. Out of them, x-rays, MRIs, and nuclear medicine scans have been used to detect cancerous tissues for a long time. However, they usually have high costs and long process times. Advancements in medical science and visual computing have enabled the development of new methods and models for cancer research, including PET-CT, CAD, CNN, and ST-Net algorithms, as efficient alternatives for the old methods.

Visual Computing Models in Cancer

Positron Emission Tomography/Computed Tomography (PET/CT)

Positron Emission Tomography (PET) is a medical imaging test using a radioactive drug as a tracer to analyze the normal and abnormal metabolic and biochemical activities carried throughout the body. During the past

decade, the application of PET scans in cancer has risen rapidly due to its effectiveness in the detection of abnormal metabolic activities before symptoms of a disease start to occur. However, being difficult to localize the radioactive drug uptake and the possibility of misinterpretation of a biological accumulation as a pathologic area are the primary disadvantages of PET scans (Zangheri et al 2004).

On the other hand, computed tomography (CT) is an imaging test using X- rays to produce images of the target body parts taken from different angles which are then analyzed by the computer for the creation of cross-sectional images of these body parts (Zhu, et al. 2019). CT scans are generally preferred against x-rays over the last decade since they provide more detailed information than x-rays do. Nevertheless, CT has the possibility of being subjected to interobserver variability, resulting in a disadvantage (Sebastian et al. 2019).

A new approach in computational medicine has been developed that not benefits from PET and CT scans but also improves them by minimizing their own limitations: PET/CT. PET/CT is a multimodal image test consisting of a combination of PET and CT scans. The research has demonstrated that a combination of PET and CT can improve each of their accuracies and can have a more effective performance than PET and CT alone. Compared to CT alone, more functional and detailed information can be added to morphological data, and compared to PET alone, PET/CT has a higher accuracy in localizing the biological areas of tracer uptake and a shorter scanning and image acquisition time (about 10 minutes shorter per patient), improving the patient comfort and reducing the possible errors due to the patient movement (Lin et al. 2009). Examples of cancer images obtained by CT, PET, and PET/CT scans are shown in Figures 1 and 2:

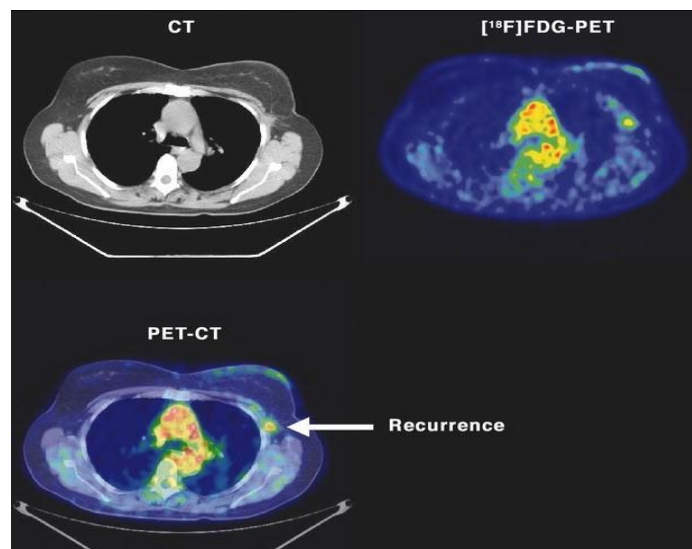


Figure 1. Detection of metastasis in mammary images of a breast cancer patient obtained by using CT, FDG-PET, and PET/CT scans. ([¹⁸F]-FDG is the abbreviation of ¹⁸F-fluorodeoxyglucose radioactive tracer used in the PET scan.) Adapted from: <https://link.springer.com/article/10.1007/s00259-004-1536-7#Sec3>

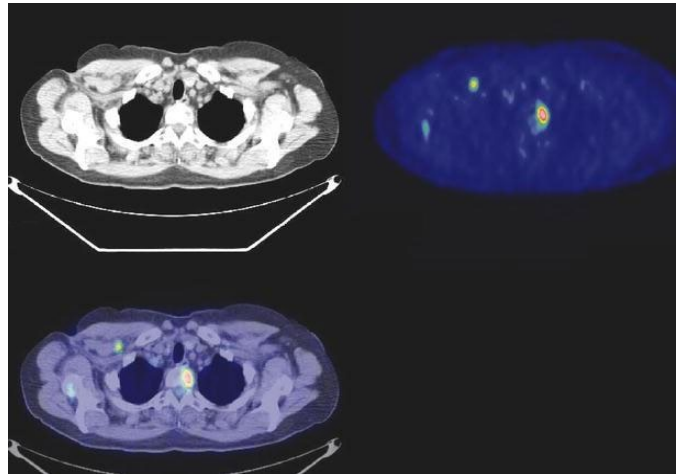


Figure 2. Detection of metastasis in supraclavicular lymph node images of a breast cancer patient obtained by using CT (top left), FDG-PET (top right), and PET/CT scans (bottom left). Adapted from: <https://link.springer.com/article/10.1007/s00259-004-1536-7#Sec3>

Results have shown that PET/CT scans are more accurate and efficient for tumor staging compared to either PET alone or CT alone (Zangheri et al. 2004), which indicates PET/CT scans have the capacity to develop the clinical practices in various malignancies. Studies have supported that they can be used effectively for screening and tracing many cancer types, including breast, prostate, lymphoma, rectal, cervical, and lung cancer. In addition, it opens the door to monitor not only cytotoxic but also predominantly cytostatic cancer therapies as an accurate response biomarker and a less costly method compared to other targeted therapy methods. It holds a promising future for the development of understanding tumor biology (Saif et al. 2010).

Computer-Aided Detection (CAD)

The use of computers in the detection of cancerous tissues has increased rapidly in the last decade, allowing to detect the potential abnormalities in the body with an improved acquisition, storage, and management of medical images. Consequently, it plays a crucial role to benefit from computer programs in order to obtain better and more precise results in cancer cases.

Computer-aided detection (CAD), which is based on the application of computers in the detection of diseases, is pattern recognition software that identifies and characterizes potential abnormalities and features on radiological images by reducing errors or false estimates due to observational oversights. In CAD models, appropriate CAD algorithms are developed to search for the targeted features in an image, such as microcalcification and masses in breast cancer mammograms, and pulmonary densities in chest radiographs.

In order to develop CAD algorithms, a digital data set of the image is required for analysis. This digital data set can be obtained directly from images already in digital formats, such as the ones taken with digital mammography and CT, or indirectly from analog images, such as x-ray films, by converting them to a digital format first (Castellino, 2005).

Dean and Ilvento have conducted research composing of 104 cancer cases belonging to patients ranging from 34 to 92 years old in which they tested the number of different types of cancer cases detected by both a radiologist and CAD, either a radiologist or CAD, and neither, and compared the results to investigate the accuracy difference in detection of cancer cases by radiologists and CAD (Dean et al. 2006). The results are shown in Table 1:

Table 1. The number of cancers detected with and without using CAD. Column A indicates the number of cancer cases detected by both a radiologist and CAD, Column B indicates the number of cancer cases detected by a radiologist but not by CAD, Column C indicates the number of cancer cases not detected by a radiologist but by CAD, and Column D indicates the number of cancer cases detected by neither a radiologist nor CAD. (Dean et al. 2006)

	Column A	Column B	Column C	Column D
	Detected by Radiologist		Not Detected by Radiologist	
Type of Cancer Case	Marked by CAD	Not Marked by CAD	Marked by CAD	Not Marked by CAD
All Cancers (n=104)	76 (73.1%)	17 (16.3%)	10 (9.6%)	1 (<1.0%)
Screening Cases (n=35)	27 (77.1%)	3 (8.6%)	4 (11.4%)	1 (2.9%)
Diagnostic Cases (n=63)	45 (71.4%)	12 (19.0%)	6 (9.5%)	0 (0.0%)
Consultation Cases (n=6)	4 (66.7%)	2 (33.3%)	0 (0.0%)	0 (0.0%)

The data obtained by Dean and Ilvento has supported the idea that CAD offers a technological method to improve the performance of radiologists and increase the accuracy in the detection of cancer cases (Dean et al. 2006).

Furthermore, being able to be developed for the use of images acquired with different methods, including mammography, x-ray films, tomography, ultrasound, and MRI, broadens the appropriate application field of CAD and improves the sensitivity of the method CAD used for (Dromain et al. 2013). As a result, CAD algorithms are highly preferred to be used for research and development in medical imaging and diagnostic radiology, and therewithal, come out as a crucial tool in the approach of computational medicine (Hadjiiski et al. 2006).

Convolutional Neural Network (CNN)

CNN is a kind of deep learning algorithm which is commonly used in visual data analysis as a result of simplifying the images for a better analysis. Matching the data point distribution in the image, CNN can be adapted to many image processing tasks for automatic feature extraction (Dabeer et al. 2019). Hence, it is widely preferred to be used in the analysis of medical images, including tumor detection in MRI images, retinal lesion detection in fundus images, and nuclei segmentation in histopathological images (Gour et al. 2020).

CNN consists of an input layer of neurons, followed by multiple convolutional layers, fully connected layers, and an output layer. The neurons in a layer are connected to other neurons in the succeeding layer, and the image is analyzed by being passed through the multiple layers. In the CNN architecture, there are two major transformation types: convolution and sumsampling. During convolution, the pixels are convolved with a filter or kernel, resulting as a dot product between the image patch and kernel. Secondly, during sumsampling, the size of the pooling filter is adjusted, which provides the opportunity to reduce overfitting. At the end of these two steps, the output is classified with a high efficiency (Dabeer et al. 2019). The whole process of the CNN architecture is presented in Figure 3 below:

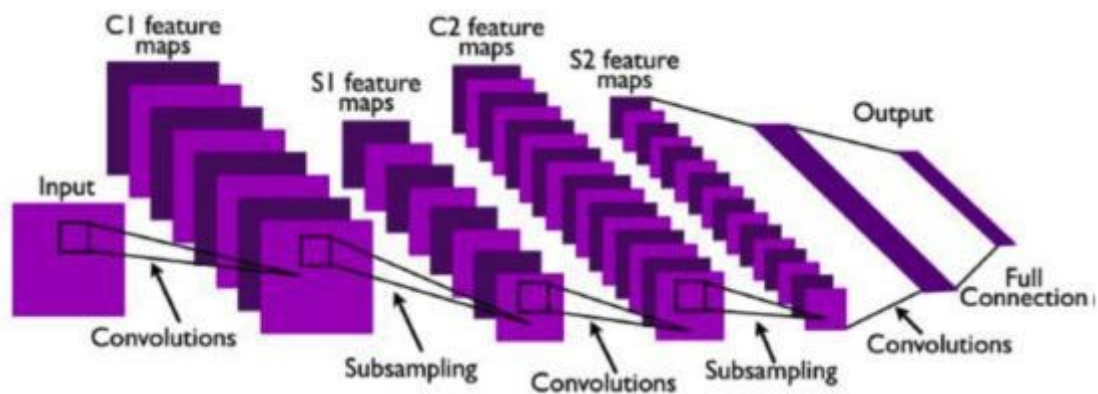


Figure 3. CNN architecture. Adapted from: <https://www.sciencedirect.com/science/article/pii/S2352914819301133?via%3Dihub>

Due to its advantages, such as extracting the features and solving the issue of signal transition, CNN is frequently used in medical image processing, including cancer research. The studies show that CNN has achieved great success in cancer classification and detection with high accuracy, especially for breast cancer and lung cancer (Alakwaa et al. 2017, Dabeer et al. 2019, Gour et al. 2020). Dabeer et. al., for instance, used input images belonging to benign and malignant tumors from the raw pixels and marked the visual patterns. They then classified them as cancer-containing and non-cancerous tissues with a classifier network and trained the CNN by using 2480 benign and 5429 malignant samples. The system presented in Figure 3 showed a 0.91 precision rate for benign tumors and 0.95 precision rate for malignant tumors, proving that CNN can be used as an effective classification model for breast cancer (Dabeer et al. 2019).

In another study, Alakwaa et. al. detected and classified lung cancer by using a different type of CNN: 3D-CNN, which works with the same process as CNN but uses and classifies 3D images instead of 2D. In the study, the 3D CNNs produced a test set accuracy of 86.6% in segmentation, detection, and classification of lung cancer (Alakwaa et al. 2017).

In addition, as CNN provides multiple model types to the users, it gives the researcher and scientists the opportunity to use different CNN models, such as AlexNet (Nawaz et al. 2018), ResNet (Jiang et al. 2019), VGGNet (Majib et al. 2021), and ST-Net, in cancer research, which broadens the application field of CNN in cancer. (More about the application of ST-Net in breast cancer has been discussed in the following part of this article.)

Cancer detection and classification by using digital images via CNN has opened a door to new opportunities in medicine for further cancer research since it proves that understanding of cancer detection can be developed by machine learning and deep learning methods. In the future scope, a combination of CNN with other imaging technologies, including MRI and mammographic images, known as the multimodel fusion technique, can also provide to obtain even better results as well as to minimize the limitations of such these traditional imaging methods (Desai et al. 2021).

ST-Net (Spatiotemporal Network)

Heterogeneity describes the differences between tumors or cancer cells, which is one of the key features of cancer (Zheng et al. 2022). Traditional single-cell techniques have provided scientists to develop a deep understanding of the biological characteristics of individual tumor cells. Nevertheless, the lack of spatial context of the transcriptome has reduced the comprehensiveness of the study of cell-to-cell interactions and limited further research on tumor heterogeneity (Monjo et al. 2022). Recent developments in spatial transcriptomics (ST) technologies have given the opportunity to profile transcriptome-wide gene expressions and gene localizations.

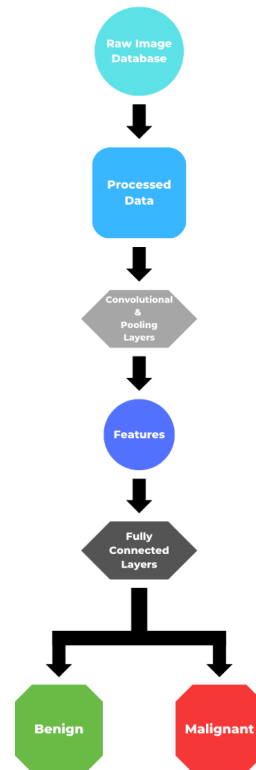


Figure 4. Dataflow diagram of CNN model

Because it is easy to obtain histology images, it is desirable to leverage information learned from ST to predict gene expressions in the availability of histology images (Pang et al. 2021).

ST-Net, composed of a CNN and three-dimensional CNN encoder, is a deep learning algorithm as an ST technology model for the prediction of local gene expression, combining spatial transcriptomics and histology images to obtain heterogeneity with high-resolution gene expression (He et al. 2020). As a newly developed algorithm, it has been tested in breast cancer, giving successful results (He et al. 2020, Patkulkar et al. 2023). In 2020, He et. al. trained the ST-Net algorithm on a spatial transcriptomics dataset of breast cancer consisting of 30,612 images from 68 breast tissue sections with the highest mean expression. In the study, they found that the predictions made by ST-Net had a root mean squared error of 0.31. Furthermore, the predicted expressions in 102 genes out of 250 correlated positively with the experimental measurements (He et al. 2020). These results suggested that a substantial number of gene expression levels can be predicted for breast cancer by using ST-Net.

Table 2. Prediction performance of ST-Net for the top five genes in breast cancer (He et al. 2020)

Gene	Number of consistent patients	Median correlation	Median correlation (smooth)	10x Correlation
GNAS	23	0.34	0.49	0.43
ACTG1	22	0.33	0.50	0.47
FASN	23	0.31	0.50	0.46
DDX5	22	0.30	0.52	0.51
XBP1	21	0.29	0.43	0.54

As a result, ST-Net has high accuracy in the prediction of spatial expression in breast cancer data without any modification, and it is more accurate and has a much higher resolution compared to other machine-learning methods using standard cellular features in the prediction of the expression.

In addition to predicting gene expression, ST-Net learns additional structure in the histopathology images, including separating the tumor tissue from normal tissue, which encourages the use of ST-Net for the large existing repositories of histology images and inferring crucial molecular biomarkers, such as tumor-immune interactions.

The findings illustrate that the combination of new spatial techniques and deep learning, such as ST-Net, can open the door for the further study of complex interactions and variations by identifying heterogeneity within a patient sample. Although this article mainly focuses on the application of ST-Net in breast cancer, it has a promising capacity to be used in other types of cancer, as well. Moreover, it can potentially develop cancer research in clinical applications as a result of its ability to enable new image-based screening of molecular biomarkers showing spatial variation (He et al. 2020).

Limitations

While visual computing offers innovative methods for the detection and classification of cancer and contributes to cancer research, each computational method discussed in this article has its own limitations in terms of different aspects.

PET/CT

Although the combination of PET and CT methods in the PET/CT model minimizes the challenges faced with PET and CT alone, it still has some disadvantages. For instance, according to the research made, there exists a possibility that some tumors are not detected with the PET/CT scans, or misinterpretations are made about tumors (Kratochwil et al. 2019). In addition, despite being at lower levels when compared to other methods, such as MRI, there is still a risk of exposure to radiation in PET/CT scans, which can lead to further issues in the patient. Composing two different imaging models, PET and CT, corresponds to longer processing times for the images obtained since more complex algorithms are required compared to single models, which might be time-consuming for the patients (Griffeth, 2005).

CAD

One of the major challenges in CAD systems is the insufficient amount of data. It is hard to acquire the analog images obtained from the systems, such as MRI and mammography, as digital images, which reduces the available digital data set. Since CAD algorithms work based on a digital data set, a lack of the data may limit the use

of data with high correctness and sensitivity levels. Moreover, CAD algorithms may have a difficulty in detecting and classifying the tumor in some cases when the density of normal and abnormal tissues are not significantly different from each other (Hassan et al. 2022).

CNN and ST-Net

CNN requires a large data set in order to classify the images accurately and precisely because CNN, as a deep learning model, classifies the images based on the training dataset. Having a limited database may increase the possibility of errors that could be seen in CNN models, acting as an obstacle to the development of CNN models (Kayalibay et al. 2017). As a CNN model, ST-Net may similarly have a limitation in accuracy due to the lack of data. In addition, since ST-Net is a new model and not enough research made about them is found, further research is needed to determine the limitations of ST-Net models more precisely and in parallel develop these models for use in cancer research.

Conclusion

Visual computing is a prominent discipline for computational medicine allowing to development of new models for cancer research in a broad spectrum. Several visual computing-based methods for the detection, segmentation and classification of cancerous tissues are currently available for medical use. In this article, PET/CT, CAD, CNN, and ST-Net models are discussed, including the previous studies made about them in the literature, their application fields in cancer research, their working mechanisms, and their limitations. In spite of the fact that some limitations are faced in each of these models, they can be minimized or overcome by further research and developments in the future. Considering the high accuracy rates in the detection and classification of tumorous tissues, visual computing models seem promising for the development of cancer research as well as for their use in the study of cancer cases.

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