2022 10th IEEE International Conference on Emerging Trends in Engineering Technology Signal and Information Processing (ICETET-SIP-22)

A Proficient Approach to Detect Osteosarcoma Through Deep Learning

Mejbah Ahammad *, Mohammad Joynul Abedin*, Md. Asiqur Rahman Khan*, Md. Abdul Alim*, Mohammad Abu Tareq Rony*, K.M. Rashedul Alam†, D. S. A. Aashiqur Reza‡, Iktear Uddin§
*Faculty of Science & Technology, American International University Bangladesh, Dhaka, Bangladesh
*Department of Statistics, Noakhali Science and Technology University, Noakhali-3814, Bangladesh
†Department of Data Science, Friedrich–Alexander University, Erlangen Nurnberg, Germany
‡Mathematics Discipline, Khulna University, Khulna, Bangladesh
§Software Engineering, Daffodil International University, Dhaka, Bangladesh
Email: 17-34760-2@student.aiub.edu*, 17-34845-2@student.aiub.edu*, 17-34907-2@student.aiub.edu*, alim.abdul.5915@gmail .com*, abutareqrony@gmail.com *, rashedulalam.km@gmail.com †, aashiq.reza007@gmail.com ‡, iktearuddinemon@gmail.com §

***Abstract*—Osteosarcoma is a life-threatening bone cancer that usually attacks young adults and children, independent of age. It habitually starts in quick-growing bone areas close to the ends of the arm or leg bones, such as the distal femur, proximal tibia, and proximal humerus. However, it can still be revealed in any bone, including the pelvis, jaw, and shoulder. The starting and the preeminent conclusion of any cancer are to identify the tumor as before long as conceivable, and it's moreover pertinent for Osteosarcoma. Osteosarcoma has a few arrange in its life cycle. The need of categorizing cancer patients into tall or short risk categories has prompted several research organizations in the biomedical and bioinformatics fields to consider using Profound Learning (Deep Learning) methodologies. Fast.ai, a Deep Learning Framework for enhancing the efficiency and accuracy of osteosarcoma tumor categorization into tumor classes, is presented in this study (tumor vs non-tumor). At the conclusion of the study, we found that employing neural networks may provide excellent precision and capability in osteosarcoma classification and model comparison.**

***Index Terms*—Osteosarcoma, Segmentation, Annotation, fastai, Augmentation, Convolutional neural network, Grad-CAM**

I. Introduction

Scientists have applied different methods to identify Osteosarcoma cancer tissues at an initial stage over the last few years. Because the early diagnosis can improve the patient's health more efficiently moreover, experts select therapy decisions based on locations, malignancy, types, and overview of the Osteosarcoma [16]. The ability to recognize cancer tissue as a small single cell is the early diagnosis requirement. Therefore, cancer cell classification is the primary research for early cancer detection and the progression and differentiation of cancer cells [20] [21].

Most of the cancer cell classification and the diagnosis depend on Hematoxylin and Eosin spotted pictures that dye the nuclei blue and the background tissues pink in a histological plane. Many inspection techniques and approaches have been specified for surgeries or respected models. However, these traditional approaches involve manual inspection of spotted planes under a microscope by physicians to approximate the magnitude of tumor and tumor necrosis [4]. The manual review is an effortful, time-consuming process and is issued to monitor bias. A diagnosis of renal cell malignancy initiated a massive argument between physicians on the identical set of data.

On the other hand, microscopic slide examination is tedious, time-costing, and may endure subjectivity [6]. Hence, it is alluring to create an automatic strategy for classifying the histopathological slide of osteosarcoma. The automated strategy is anticipated to result in reduced examination time with an increment in prediction accuracy. The entire slide checking system allows for building an instinctive analysis system [5]. These systems automate glass slides with the recoloured tissue at a high resolution (to 40). Therefore, the features of tissue classification are obtained from digital whole slide images (WSIs) by utilizing the morphological and contextual clues shown within the WSI [8].

Nonetheless, there are several roadblocks in the way of a fully automated system. To begin with, the digital image is measurable, with slide planning and destitute recolouring reaction having an impact. Many tissue and cellular areas are under-represented as a result. Second, histology images show various cellular morphologies [9]. Changeability in the same cell type and similarity in diverse cellular structures cause this.

Normal cells and osteosarcoma tumor cells are both blues in colour. Tumor cells, on the other hand, have an asymmetrical form, whereas pioneer cells are rounder, more impending, and more regular [11]. Furthermore, each tumor form is distinct from the others, making it challenging to apply a method devised for one tumor pattern to a different tumor pattern. Osteosarcoma is a tumor having a significant degree of dimensional inconstancy inside the tumor [13]. As a result, the procedures used to treat tumors of the kidneys or lungs do not work well for osteosarcoma. [19] [7].

This research used a COD-based DL approach to distinguish osteosarcoma cells from MSCs in many differentiated samples of cells cultivated on a glass slide (osteoblasts). With an accuracy of approximately 1, the findings demonstrate exceptional performance.

CNN-based classification has lately gained remarkable success in computer vision and pattern recognition, thanks to the introduction of deep convolutional neural networks (CNNs) [14]. This paper builds on our earlier work by fine-tuning and expanding the basic CNN architecture presented for classifying HE stained osteosarcoma histopathology slides. The convolution filter layers are alternated by pooling layers in a standard CNN image processing architecture. Convolution filters are used to recognize small sections of the input image. We combined Alex Net and Le-Net into the neural network architecture to construct a quick and accurate slide classification system. The suggested approach eliminates the need for nuclei segmentation, which might be challenging because of the morphological and system restrictions discussed previously. The system generates features at the class level using the annotated picture label. We may concentrate on precise and efficient class label detection instead of calculating nucleus attributes [18]. We employ several classification approaches, clustering, and a traditional strategy in this work to improve the degree of accuracy in detecting Osteosarcoma on bone tumors. First, we'll look at convolutional neural networks. Create three separate hidden layers two hidden layers, three hidden layers, and five hidden layers. However, we receive poorer accuracy (84 percent 87 percent) and a longer memory consumption time. To detect the tumor, we construct an image segmentation and annotation model. Finally, we used the fastai framework to develop a deep learning model that was 99 percent accurate. Histopathology pictures were used to identify osteosarcoma.

The system generates features at the class level using annotated, enhanced, and segmented pictures and labels. As there is no requirement to enumerate the nuclei possession, we can concentrate on perfect and proficient class label consolidation.

To assist discover if a suspicious range may well be cancer To offer assistance decide if cancer might have begun in another portion of the body To learn how distant cancer has spread To offer assistance decide if treatment is working To seek for signs that cancer might have come back [17]A biopsy can reveal trademark changes inside the tumor tissue that are indicative of Osteosarcoma. Regardless of the way that they may be normal for Osteosarcoma, different conditions can make these synthetic compounds tall. These blood tests can't investigate Osteosarcoma [18]. First of all, we have created two separate models one is to detect the Targeted cancer bone which is known as Osteosarcoma, One of the models is Convolutional Neural Network with Tensor Flow API and another one is fastai API then we have compared both the model and pick the best one of them. We saw that the others worked on exactly one specific model to detect this bone cancer, but we worked with different models or approaches to peak the best model. Here, we want to propose a comprehensive analysis to find out the bone tumor cell-associated with Osteosarcoma cancer and we predicted an approach to detect osteosarcoma through deep learning.

II. Related Works

The papers suggest a strategy to improve the quality and accuracy of the classification of osteosarcoma tumors in classes of the tumors versus nontumor, the Convolutional Neural Network [7]. Three sets of stacked two coevolutionary layers interspersed with max-pooling layers to remove features and two fully connected layers with data increase strategies for performance enhancement make up the proposed CNN architecture. The application of a neural network [15] yields a higher rating accuracy of 92 percent. This study looked into the value of multi-parametric magnetic resonance imaging mixed with machine learning for assessing tumor necrosis following NACT for osteosarcoma [2]. As viable tumor zones and tumor zones, 102 pathologically characterized tissue samples have been acquired. Individual tumor survival, non-cartilaginous tumor survival, and cartilage tumor survival were all classified using three different methods. [7]

TABLE I: Related Research

Features	D'Acunto [1]	Huang [15]	Sujatha [3]	Proposed
Fastai	×	×	×	✓
CNN	✓	×	✓	✓
Grad-CAM	×	×	×	✓

For extremities sarcomas, the Enneking methods for staging malignant musculoskeletal tumors and the American Joint Committee on Cancer (AJCC) staging systems are the most widely utilized.

The Enneking techniques for staging malignant musculoskeletal tumors and the American Joint Committee on Cancer (AJCC) staging systems are the most extensively used for sarcomas of the extremities. In the paper "Histopathological diagnosis for viable and non-viable tumor prediction for Osteosarcoma using convolutional neural network," they proposed a CNN design that includes five learned layers, three convolutional layers mixed with max-pooling layers for include extraction, and two fully-connected layers with information increase procedures to boost execution [10]. This [14] study, "Segmentation of Multimodality Osteosarcoma MRI Using Vectorial Fuzzy-Connectedness Theory," speeds up the segmentation process by segmenting two Osteosarcoma tissues at once.

III. Brief information about Osteosarcoma

A. *Symptoms of Disease:*

Osteosarcoma is the most frequent type of bone cancer, and it affects mostly teenagers. The pain and swelling of the damaged bone are the first signs of osteosarcoma, and the symptoms are generally worst at night. Furthermore, when the tumor is in the lower knee, limp or other difficulties may ensue. The most typical symptoms in the tumor location include bone discomfort, edema, and redness.

B. *Classification of Disease:*

Osteosarcomas are classified as primary and secondary [12]. Like other primary bone tumors, primary osteosarcoma originally comes from bone cells, and also this is not directly associated with any other cancer or disease which occurs in young patients (10-25 years).

It thrives in the metaphyseal areas of long bones, with a particular fondness for the knee. After radiation exposure and Paget's disease, secondary osteosarcoma can develop in the elderly. It has a wider distribution, with a higher prevalence in flat bones, particularly the pelvis, although it is also linked to a skeletal illness or therapy for another ailment (typically cancer).

C. *Risk factors of Osteosarcoma:*

Diverse infections like cancer have diverse hazard components. There are numerous sort of components like age, gender, sex, Race/Ethnicity, body weight, height, radiation of Bone, physical Movement, Eating less, Tobacco use, Bone structure, etc. A few variables of Osteosarcomas are- The chance of Osteosarcoma is most for matured individuals between 10 and 30. This hazard gets darkened at the centre age and once more in more seasoned age it has the tall chance to be getting caught with Osteosarcoma. It influenced individuals to be taller than their age. It is generally seen in male individuals more than females. Since a male persons' bone development is quicker than that of a female individual. It is generally seen in Americans and Latinos more than the other individuals of the world. The chance to create cancer like Osteosarcoma within the zone of already treated cancer with radio treatment. It has more chance to create cancer if the radiotherapy is given at a more youthful age.

D. *Diagnosis options for Osteosarcoma:*

An X-Ray is a Primary test that is used for Osteosarcoma patients. There are several other tests that can be used for Osteosarcoma patients Like:

1) A MRI of the entire bone where the problem is more likely.
2) A City scan or an x-ray of the chest will help to find the chest metastases.
3) The entire body bone scan for the prevention of cancer.
4) A biopsy test can be done which will help to detect cancer and also help to find out the grade of cancer (low grade or high grade).

There are mainly two types of biopsy:

- A Needle Aspiration
- A Surgical biopsy

The result of the biopsy will provide the physicians with an idea about the nature, stage, and grade of the disease. Then the physicians will take action against the disease based on those parameters.

IV. RESEARCH METHODOLOGY

In this section, we define the basic step of AI architecture. We conclude this by explaining the approach taken to strengthen and expand the baseline to produce improved performance.

A. *Data Collection and Overview*

The dataset includes photographs of hematoxylin and eosin (HE) stained osteosarcoma histology. A group of clinical scientists at the University of Texas Southwestern Medical Center in Dallas gathered the information. This dataset was created using samples from 50 kids treated at the Children's Medical Center in Dallas between 1995 and 2015. Pathologists picked four patients (out of 50) based on various tumor specimens following surgery. Based on the prevalent kind of cancer in each picture, the images are classed as Non-Tumor and Tumor. Two medical specialists contributed to the annotation. Two annotation pathologists shared all of the photos. Because a single pathologist annotated each picture, each image had only one annotation. The dataset contains 1144 photos, evenly distributed between 852 non-tumor images and 292 tumor images.

B. *Data Preprocessing:*

Firstly, we create a CSV file with all images features. We also divide our image dataset into two separate folders one for training and another one for testing/validating images. We took 80% of the images for training and 20% for testing.

TABLE II: First Five Rows of the Feature Dataset.

image.name	X.x	Blue.count	Classification
Case3...25283	548	16611	0
Case3...20223	550	107853	0
Case3...17155	25	122760	1
Case4...16377	150	65935	1
Case4...20389	162	60328	0

C. *Applying Model*

Image enhancement is the method of controlling an image. The need for this process is to enhance the image so that the picture will be more readable and can be used for better accuracy. We have used the color of the image to extract the feature that we need. We have also used the method of image segmentation and this is why we can easily find out the materials from the image that gives us the more appropriate and accurate result. We have used fastai API to create our main model for the detection of tumors from osteosarcoma image datasets.

1) Image Augmentation : There are a couple of ways we will utilize to maintain a strategic distance from overfitting more data, augmentation, regularization, and less complex demonstrate designs. Here, we are going to characterize what picture increases to utilize and include them straightforwardly in our picture loader work (Fig.3). Note that if we apply expansion here, enlargements will moreover be connected

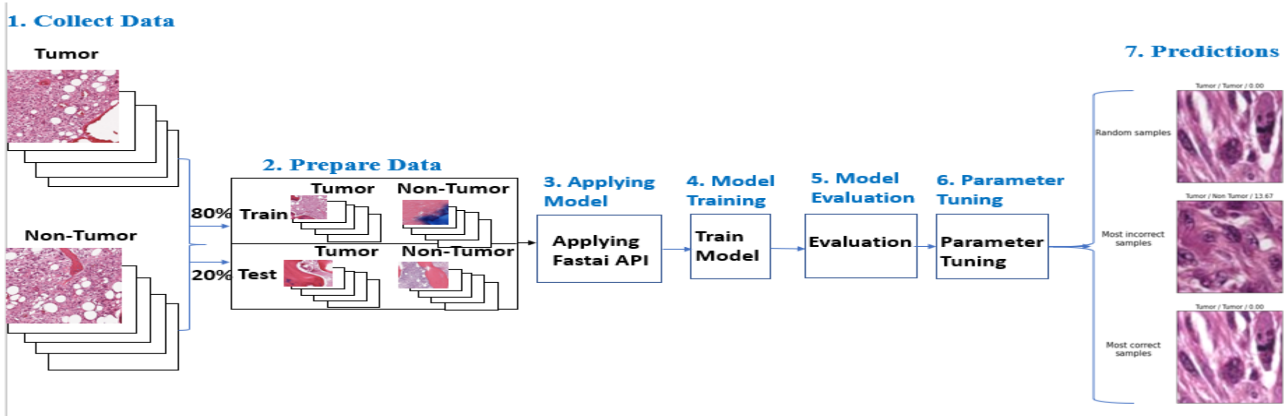

Fig. 1: Proposed Methodology

Fig. 2: Image Combinations

when we are foreseeing (induction). This can be called test time increase (TTA) and it can progress It comes about the case we run induction at different times for each picture and normal out the forecasts.

2) Image Annotation: Picture comment may be a key technique utilized to make planning data for computer vision. In organising for machines to see objects in their environment, clarified pictures are required to get ready Machine Learning calculations to memorize to see the world as we do.

TABLE III: Locations of targeted features

S/N	X	Y	Viability
0	421	333	True
1	768	633	False
2	287	175	True
3	955	320	False
4	696	68	True
5	267	259	False

Comment in Machine Learning is essentially the strategy of naming data inside the different mediums of pictures, substance, or video. The names are more frequently than not foreordained by a machine learning plan or computer vision analyst and are chosen to supply the computer vision appearance information on objects depicted in a picture. Here, we have characterized practical tumors as genuine and non-practical tumors as wrong.

3) Convolutional Neural Network design: Convolutional neural networks are effective learning tools with a high success rate in image categorization. The standard CNN structure for image classification consists of a series of convolution channels that are coordinated with pooling layers. To distinguish dynamically relevant visual highlights, such as edges, forms, and surfaces, the convolution channels are coupled with discrete regions of the input picture (Fig.7). One or more probabilities or lesson names are the CNN's output. [15]

- **Input:** This will save the picture's raw pixel values, which will be a picture with a width of 128, a height of 128-, and three-colour channels of R, G, and B. [128 128 3] is the input volume.
- **Convolution:** The yield of neurons associated with local localities within the input picture will be computed by this layer. Each neuron will compute the speck item using their weights and a little area inside the input volume to which they are connected. For four filters, this may result in a volume of [124 124 4].
- **Max pooling:** This layer will calculate the yield of neurons linked with certain places in the input image. Using their weights and a little region inside the input volume to which they are attached, each neuron will calculate the speck item. This might provide a volume of [124 124 4] for four filters.

4) Image segmentation: will partition or segment the picture into different parts called segments. It's not an extraordinary thought to handle the complete image at the same time as there will be districts within the picture which don't contain any data. By isolating the picture into fragments, ready to make utilize the critical sections for handling the picture. That in a nutshell is how picture division works. A picture could be a collection or set of distinctive pixels (Fig.8). We bunch together the pixels that have comparable properties utilizing picture division. [15]

5) Grad-CAM: This strategy (Gradient-weighted Class Activation Mapping) produces a coarse localization outline highlighting the ranges that the show considers imperative for the

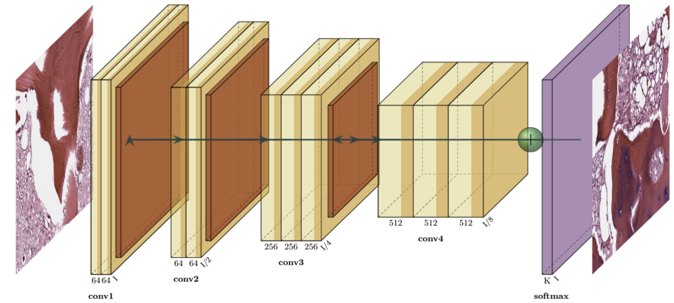

Fig. 3: CNN Design For Osteosarcoma

classification choice. The visual clarification gives straightforwardness to the show making it simpler to take note if it has learned the off-base things. In case we would prepare a puppy breed classifier and all of our pictures of a certain pooch breed would have been taken in a pooch appearance competition. There's a great chance that the demonstrate would learn to recognize the competitive environment rather than doggy highlights with that breed. Visualizing the localization outline would uncover that we seem to centre on getting more different information about that breed.

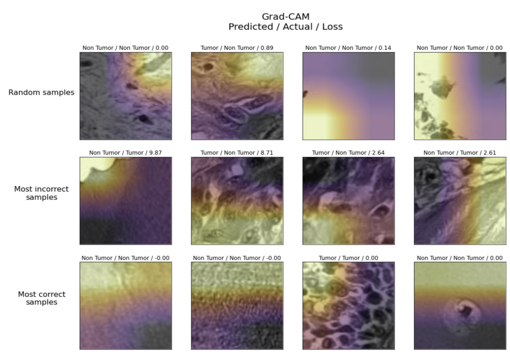

Fig. 4: Gradient-weighted Class Activation Mapping

6) Fastai : Fastai is a deep-seated learning library that provides high-level components to professionals so that they may rapidly and effectively provide state-of-the-art results in deep learning domains, as well as low-level components to researchers so that they can incorporate fresh methodologies.

An interesting key feature of Fastai is to separate the item level and batch level transformation. This feature performs the task in both CPU and GPU. It uses the CPU to process the item level whereas the GPU is used for the batch level transformation if available because Fastai allows data augmentation to perform on the GPU.

For data loading, the data block API is an interactive API. We are conscious of explaining all the steps needed to prepare data for a deep learning model, as it is our first attempt. The steps that the data block API described are: i)Collecting the source objects ii)Splitting the objects into the training set and one or more testing sets iii)Labelling the objects iv)Processing the objects (such as normalization) v)Collating the objects into batches optionally.

D. Model Evaluation

To evaluate the model more perfectly in run time we have augmented our images which might be improved but if we do predictions multiple times per image and average the results then the probability ranges will be between 0 and 1.In order to evaluate our model we have considered the terms that are written below,

- Accuracy: how well the model performed in comparison to a benchmark;
- Robustness: The capacity of a model to withstand a variety of situations;
- Sensitivity: how adaptable a model is too small changes in feature attributes;
- Adaptability: how the model handles image variability;
- Reliability: when a model is run with the same stable data, the degree to which it produces the same result;
- Efficiency: the model's practical practicality (in terms of time and space).

TABLE IV: Locations of targeted features

epoch	train_loss	valid_loss	accuracy	time
0	1.383397	0.889030	0.800000	00:16
1	1.107034	2.355759	0.617391	00:15
2	0.879058	0.490067	0.826087	00:14
3	0.754707	0.652697	0.773913	00:14
4	0.670129	0.594402	0.843478	00:16
5	0.613961	0.446206	0.843478	00:15

1) Confusion Metrix: : The course labelled 1 is the positive lesson in our illustration. The lesson labelled as is the negative here. As we will see, the positive and negative real values are spoken to as columns, whereas the anticipated values have appeared as the columns.

V. Result and Discussion

Firstly, We have created the convolutional neural network to detect Osteosarcoma with the Keras API and **Conv2D layer** method. Here, the accuracy rate for two hidden layers is 93% and 96% for three hidden layers and 84% for five hidden layers. First of all, we train our images and compare them with our testing image dataset. After comparing those images, we calculated the loss to identify the Tumor and Non-Tumor images.

Next, Image Augmentation and Image segmentation approaches are built to identify bone tumor cells from the image datasets. In this process, we convert all of the images into a mask or labelled images. We use this process to know the exact position of the tumor in the cell. We have also used another deep learning framework called Grad-CAM to detect the target features. This approach helps create a high-resolution class-discriminative visualization. Fastai is used in our model to detect the osteosarcoma-affected bone with greater accuracy

TABLE V: Comparison of different Model

Model Name	Accuracy
CNN:2 layers	93%
CNN:3 layers	96%
CNN:5 layers	84%
MSFCN	87.80%
ADC	93%
Multi-parametric	97%
Fastai	99%

than the previous models we've studied and created. Based on our analysis with fastai, we agreed that the use of a layered API in deep learning has incredibly important advantages for analysts, practitioners, and undergraduates. Analysts can see joining over distinctive ranges more effortlessly, quickly combining and rebuilding thoughts, and running tests to beat solid baselines. Professionals can quickly build models, and refine those models by using fastai's PyTorch establishments, without renovating the code. Understudies should test the styles and try the varieties, without getting overpowered by the boilerplate code when they start studying the thoughts.

VI. Conclusion and Future work

In this article, We proposed a proficient approach using fastai to detect Osteosarcoma tumor cells. The proposed methodology is reliable, accurate, and focused only on the exact position of the tumor on the osteosarcoma cell images. To begin, medical domain specialists manually assess the training and testing photos. Perhaps this is the first work where we try to detect Osteosarcoma by using fastai. The datasets and resources that we have used in our work are still in public. We can create or build another architecture for detecting Osteosarcoma but it will bring more cost. Able to proceed to explore diverse models and methodologies for the preparing of neural networks by changing the hyperparameters or utilizing the engineering for highlight extraction and classifying as it were on the premise of relevant features.

References

[1] M. D'Acunto, M. Martinelli, and D. Moroni, "Deep Learning Approach to Human Osteosarcoma Cell Detection and Classification," Cryptology and Network Security Lecture Notes in Computer Science, pp. 353–361, Jan. 2018.

[2] Huang, Bingsheng, et al. "Feasibility of multi-parametric magnetic resonance imaging combined with machine learning in the assessment of necrosis of osteosarcoma after neoadjuvant chemotherapy: a preliminary study." BMC cancer 20.1 (2020): 1-9.

[3] K. Sujatha, S. Jayalakshmi, P. Sinthia, M. Malathi, K. Ramkumar, S.-Q. Cao, and K. Harikrishnan, "Screening and Identity the Bone Cancer/Tumor using Image Processing," 2018 International Conference on Current Trends towards Converging Technologies (ICCTCT), 2018.

[4] Takafumi, Osteosarcoma. Place of publication not identified: SPRINGER Verlag, JAPAN, 2018.

[5] Baidya Kayal, Esha, et al. "Segmentation of osteosarcoma tumor using diffusion weighted MRI: a comparative study using nine segmentation algorithms." Signal, Image and Video Processing 14.4 (2020): 727-735.

[6] Arunachalam, Harish Babu, et al. "Viable and necrotic tumor assessment from whole slide images of osteosarcoma using machine-learning and deep-learning models." PloS one 14.4 (2019): e0210706.

[7] R. Mishra, O. Daescu, P. Leavey, D. Rakheja, and A. Sengupta, "Convolutional Neural Network for Histopathological Analysis of Osteosarcoma," Journal of Computational Biology, vol. 25, no. 3, pp. 313–325, Mar. 2018.

[8] Anisuzzaman, D. M., et al. "A deep learning study on osteosarcoma detection from histological images." Biomedical Signal Processing and Control 69 (2021): 102931.

[9] Y. Fu, P. Xue, H. Ji, W. Cui, and E. Dong, "Deep model with Siamese network for viable and necrotic tumor regions assessment in Osteosarcoma," Medical Physics, Aug. 2020.

[10] Mishra, Rashika, et al. "Histopathological diagnosis for viable and non-viable tumor prediction for osteosarcoma using convolutional neural network." International Symposium on Bioinformatics Research and Applications. Springer, Cham, 2017.

[11] Alfranca, Arantzazu, et al."Bone microenvironment signals in osteosarcoma development.Cellular molecular life sciences72.16(2015): 3097-3113.

[12] Kundu, Zile Singh. "Classification, imaging, biopsy and staging of osteosarcoma." Indian journal of orthopaedics 48.3 (2014): 238-246.

[13] V. Higuera, "Osteosarcoma: Symptoms, Tests & Treatments," Healthline, 31-Mar-2017. [Online]. Available: https://www.healthline.com/health/Osteosarcoma.

[14] Ma, Jing, Minglu Li, and Yongqiang Zhao. "Segmentation of multi-modality osteosarcoma mri with vectorial fuzzy-connectedness theory." International Conference on Fuzzy Systems and Knowledge Discovery. Springer, Berlin, Heidelberg, 2005.

[15] Huang, Lin, et al. "MSFCN-multiple supervised fully convolutional networks for the osteosarcoma segmentation of CT images." Computer methods and programs in biomedicine 143 (2017): 67-74.

[16] Lindsey, Brock A., Justin E. Markel, and Eugenie S. Kleinerman. "Osteosarcoma overview."Rheumatology and therapy 4.1(2017):25-43.

[17] Braz, Isaac Felipe Leite, et al. "Analysis of cancer perception by elderly people." Einstein (Sao Paulo) 16 (2018).

[18] Fuchs, Thomas J., et al. "Computational pathology analysis of tissue microarrays predicts survival of renal clear cell carcinoma patients." International Conference on Medical Image Computing and Computer-Assisted Intervention. Springer, Berlin, Heidelberg, 2008.

[19] Fuchs, Thomas J., et al. "Computational pathology analysis of tissue microarrays predicts survival of renal clear cell carcinoma patients." International Conference on Medical Image Computing and Computer-Assisted Intervention. Springer, Berlin, Heidelberg, 2008.

[20] Song, Q., Merajver, S.D., Li, J.Z.: Cancer classification in the genomics era: ve contemporary problems. Human Genomics 9 (2015)

[21] Idikio, H.A.: Human cancer classification: A systems biology-based model integrating morphology, cancer stem cells, proteomics, and genomics. Journal of Cancer 2 (2011)