Research Article

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Osteosarcoma Tumor Detection using Different Transfer Learning Models

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ABSTRACT

The clinical image analysis field has increasingly embraced the utilization of transfer learning models due to their reduced computational complexity and improved accuracy, among other benefits. These models, which are pre-trained and do not require training from scratch, eliminate the need for extensive datasets. While transfer learning models are primarily employed for brain, breast, or lung image analysis, other areas such as bone marrow cell detection or bone cancer detection can also derive advantages from their use, particularly considering the limited availability of large datasets for these specific tasks. This research paper investigates the performance of various transfer learning models for the detection of osteosarcoma tumours, a form of bone cancer predominantly found in the long bones of the body's cells. The dataset comprises histopathology images stained with H&E, categorized into four groups: Viable Tumor, Non-viable Tumor, Non-Tumor, and Viable Non-viable. The datasets were randomly split into training and test sets, following an 80-20 ratio, with 80% used for training and 20% for testing. Four models were evaluated for comparison: EfficientNetB7, InceptionResNetV2, NasNetLarge, and ResNet50. All these models were pre-trained on ImageNet. According to the results, InceptionResNetV2 achieved the highest accuracy (93.29%), followed by NasNetLarge (90.91%), ResNet50 (89.83%), and EfficientNetB7 (62.77%). InceptionResNetV2 also exhibited the highest precision (0.8658) and recall (0.8658) values among the four models.

INTRODUCTION

Early detection of osteosarcoma, a prevalent form of bone cancer with a grim prognosis, holds immense significance. Meltzer et al.[1] reported that osteosarcoma represents the most frequently encountered malignant bone cancer and is the earliest known hominin cancer across the globe. Survival rates indicate a 5-year average for approximately 60% of patients, whereas those with metastatic lung diseases face a mere 20% chance of survival. Adolescents and individuals between the ages of 10 and 30 exhibit the highest susceptibility to developing osteosarcoma tumours, primarily in regions of longitudinal bone growth such as the Distal Femur and Proximal Tibia (Knee) or Proximal Humerus (Shoulder). Notably, individuals over the age of 60 have the second highest risk, often associated with Paget's disease of the bone, suggesting a distinct biological process at play. The severity of this condition has also been documented in Bangladesh, where Begum KNA et al.[29] highlight its rank as the third most frequently occurring malignant cancer. These findings underscore the critical importance of accurately detecting osteosarcoma tumours to facilitate appropriate treatment interventions.

Medical image analysis plays a pivotal role in enabling accurate diagnosis and appropriate treatment by identifying and categorizing specific elements or characteristics in medical images[14]. Utilizing computer-based image processing techniques, involves the classification, feature extraction, reconstruction, and presentation of organs or tissues suspected of being affected by various diseases. These images can be in 2D or 3D format, and by analyzing their similarities and dissimilarities, experts can effectively detect medical issues, significantly improving the precision and reliability of diagnoses[15]. Commonly employed tasks in medical image analysis include visualization, segmentation, and enhancement, with evaluation criteria such as recall, sensitivity, precision, specificity, and F-measure used to ensure accuracy[14]. The segmentation technique offers the advantage of remote image analysis, reducing computational complexity, time, and cost by eliminating the need for

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biological samples in the segmentation process[16].

The diagnosis of osteosarcoma heavily relies on the examination of radiographic images that capture the affected areas. To assess the extent of tissue and bone involvement, various cross-sectional imaging techniques are employed. CT scans and MRI images are commonly used for this purpose, although MRI is favoured due to its superior ability to reveal conditions such as soft tissue extension, localized intramedullary metastases, and intramedullary beating metastases, among others[17]. Once the tumour is detected, doctors can enhance the quality of treatment by evaluating the tumour's response to chemotherapy. Tumour necrosis has long played a significant role in the treatment of high-grade osteosarcoma[18].

Early detection of osteosarcoma and vigilant monitoring significantly improve the chances of patient survival. However, in developing countries like Bangladesh, where there is a scarcity of qualified radiologists, this crucial facility is often unavailable to patients. Moreover, the detection of osteosarcoma is a challenging and time-consuming process that involves grading cancer and necrosis cells during treatment, often requiring the involvement of multiple radiologists[19]. Furthermore, the accuracy of detection is reliant on the experience and expertise of the individuals involved, making a computerized approach preferable to manual detection. Several factors can influence the output. Firstly, tumours exhibit variations in shape, size, and structure. Secondly, the highly heterogeneous nature of this cancer type introduces additional complexity, as the uneven density distribution between tumour cells and normal cells makes differentiation challenging[20].

Given the intricacy and challenges involved in osteosarcoma detection, computerized diagnostic methods are preferred due to their ability to provide accurate results (distinguishing between malignant and benign tumours) while reducing complexity. These approaches involve feature extraction, a technique that aims to explain data by reducing its dimensionality. However, the complexity of this process increases when dealing with complex input images. To address this, Deep Learning (DL) models can be employed as feature extractors. These models utilize faster and more compact processors, coupled with Convolutional Neural Networks (CNNs), which minimize the need for extensive image pre-processing. However, one major drawback of this approach is the requirement for large training datasets to prevent overfitting[2].

Transfer Learning (TL) is a technique within Deep Learning that involves pre-training models to perform one task, which can then be applied to related tasks. There are two main approaches to implementing transfer learning: utilizing a general image pre-trained network or a medical image pre-trained network for fine-tuning[21]. This method has gained attention in computerized medical image analysis, as it allows for the utilization of previously initialized weights, resulting in improved accuracy when trained with a large dataset. Instead of building the same model repeatedly, transfer learning enables the use of weights trained on one dataset to classify another dataset[22].

One popular training method for transfer learning models is the ImageNet database, which provides a publicly available collection of over 14 million manually annotated images, including around one million images with bounding boxes. Transfer learning involves leveraging knowledge acquired from one domain to enhance optimization in another domain. The process entails using a deep Convolutional Neural Network (CNN) model previously trained on a sizable dataset. A new dataset, with fewer training images than the original dataset, is then used to further train (fine-tune) the CNN model. Typically, the initial layers of the CNN learn low-level features like edges and curves, while the later layers focus on more abstract features. Often, the fully connected layer, SoftMax layer, and classification output layer are replaced, while the remaining layers are retained for the new classification task[23].

Transfer learning eliminates the need for large datasets to train models from scratch with randomly initialized weights, making it an effective choice when the available dataset is limited[3]. **Figure 1** illustrates the concept of transfer learning:

Figure 1

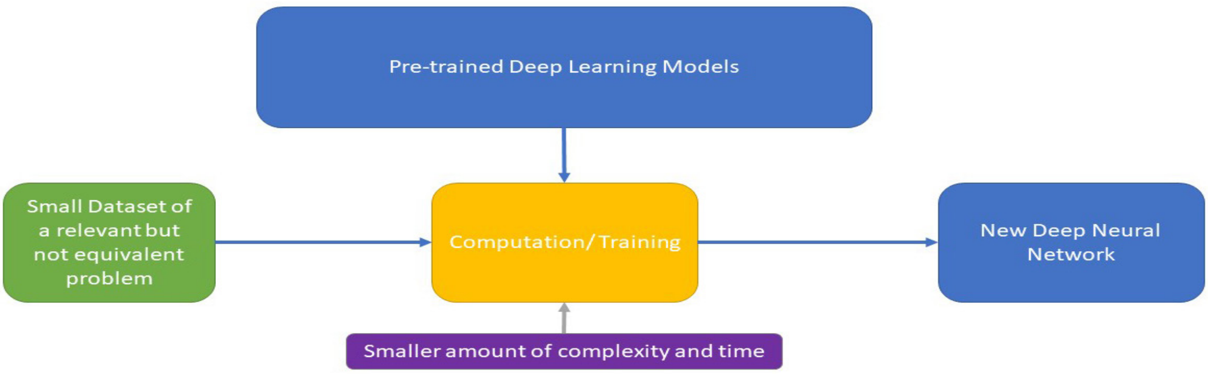

Figure 1. Transfer Learning Architecture.

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This paper focuses on the application of four pre-trained transfer learning (TL) models, namely EfficientNet, InceptionRes Net, NasNet, and ResNet, to detect Osteosarcoma tumours using a small dataset. The selection of these models is based on their performance on relevant tasks, which will be discussed in subsequent sections. The paper is structured into five sections. Section II provides an overview of the current advancements in this field. Section III presents an analysis of the results obtained. Section IV outlines the methods and materials employed in this study. Finally, Section V concludes the paper and highlights potential avenues for future research.

LITERATURE REVIEW

Deep Learning (DL) and Convolutional Neural Networks (CNN) have been extensively utilized in medical image segmentation for many years. In this field, Transfer Learning (TL) has gained significant attention as it offers a solution to the need for large training datasets. Morid et al.[4] conducted a scoping review to explore different TL models trained on the ImageNet dataset for medical image analysis. The study focused on articles published after 2018 to provide the most up-to-date information. The research identified commonly used TL models specific to different types of medical images. For instance, Inception models were frequently employed for X-ray, endoscopic, or ultrasound images, while VGGNet showed better performance for OCT or skin lesion images. Overall, the top four frequently used models, regardless of image or organ type, were Inception, VGGNet, AlexNet, and ResNet. The InceptionResNet model, being a newer approach, was mentioned in only three studies. The preference for Inception and ResNet models was also supported by the literature review conducted by Kim, Hee E., et al.[5].

Shah, Hasnain Ali, et al.[6] proposed an approach using the TL model EfficientNet for Brain Tumor Detection with MRI images. The method employed the EfficientNetB0 model pre-trained on the ImageNet dataset. They also compared the outputs with five other TL models: VGG16, InceptionV3, Xception, ResNet50, and InceptionResNetV2. Adjusted coefficients were used to enhance the dimensions of the EfficientNet model, leading to superior performance compared to other Deep CNN models. An optimizer algorithm was employed to modify biases and learning rates, resulting in increased accuracy and reduced overall loss. The proposed approach achieved a detection accuracy of 98.87%.

Marques et al.[7] also utilized EfficientNet, specifically EfficientNetB4, for the classification of COVID-19 medical images. The study focused on binary classification of COVID-19 patients versus healthy patients, as well as multi-class classification involving COVID-19, pneumonia, and healthy patients. To mitigate overfitting, the proposed method introduced a "global_average_pooling2d" layer and implemented three inner dense layers with RELU activation functions and dropout layers. The SoftMax activation function was used in the output dense layer for classification. The average accuracy of the model for binary and multi-class classification was 99.62% and 96.70%, respectively.

Falconi et al.[8] conducted experiments to assess the accuracy of MobileNet and NasNet for the classification of Breast Mammogram Abnormalities. They created sub-datasets, including the Otsu Dataset for image segmentation using Otsu's algorithm and the ROI dataset containing tissue information. In addition to MobileNet and NasNet, they also employed InceptionV3 and ResNet50 for comparison. For the Otsu dataset, NasNet (68.0%) and InceptionV3 (67.5%) achieved the highest accuracy, while ResNet50 (78.4%) and MobileNet (74.3%) performed best for the ROI dataset. Faruk et al.[9] conducted a comparative study on four transfer learning (TL) approaches- Xception, InceptionV3, Inception ResNetV2, and MobileNetV2- for tuberculosis detection from X-ray images. Each model consisted of a specific architecture, including flattened layers, dense layers with ReLU activation, MaxPooling2D levels, and Conv2D layers. Among the four models, InceptionResNetV2 achieved the highest accuracy (99.36%). In a similar context, Demir and Yilmaz[25] focused on pneumonia detection using X-ray images and specifically preferred the InceptionResNetV2 model. They made modifications such as replacing ReLU activation with LeakyReLU activation and using Averagepooling layers instead of Maxpooling. They experimented with different combinations and observed that InceptionResNetV2 with LeakyReLU had better accuracy and specificity compared to the other models.

Anisuzzaman et al.[10] explored the use of VGG19 and InceptionV3 deep learning models for osteosarcoma detection in histological images. They made adjustments to the models by adding and modifying layers, including fully connected layers with ReLU activation, dropout layers to prevent overfitting, and SoftMax activation in the output layer. The VGG19 model achieved high accuracy for both binary and multiclass classifications.

Mahore et al.[11] proposed a Random Forest machine learning algorithm for osteosarcoma detection and compared it with deep learning models like VGGNet, CNN, AlexNet, and LeNet. They utilized expert-guided features and Cell-profiler features, achieving an accuracy of 92.4% with their proposed method.

Nasir et al.[2] introduced a transfer learning model for automatic osteosarcoma cancer detection, incorporating blockchain technology and fog and edge computing. They followed a five-layer paradigm, including data collection, pre-processing, edge computing, fog computing, and testing. With a large dataset of whole-slide images, their model achieved an accuracy rate of 99.3%.

Sarwinda et al.[12] compared two variants of ResNet- ResNet-18 and ResNet-50- for benign and malignant colorectal cancer detection. The models underwent pre-processing steps, followed by the utilization of residual blocks and classification layers. ResNet50 outperformed ResNet18 in terms of accuracy, sensitivity, and specificity. Ma et al.[26] applied ResNet combined with Deep Convolutional Generative Adversarial Network (DC-GAN) for blood cell classification. They introduced a state-of-the-art loss function and employed DC-GAN for sample expansion. The proposed model achieved an accuracy of 91.68% and demonstrated robustness in handling small datasets or anomalies in the dataset. In summary, TL models have been extensively used in brain and lung disease detection, particularly in various types of cancer. They have shown impressive performance in osteosarcoma detection, encouraging further research in this domain.

METHODS

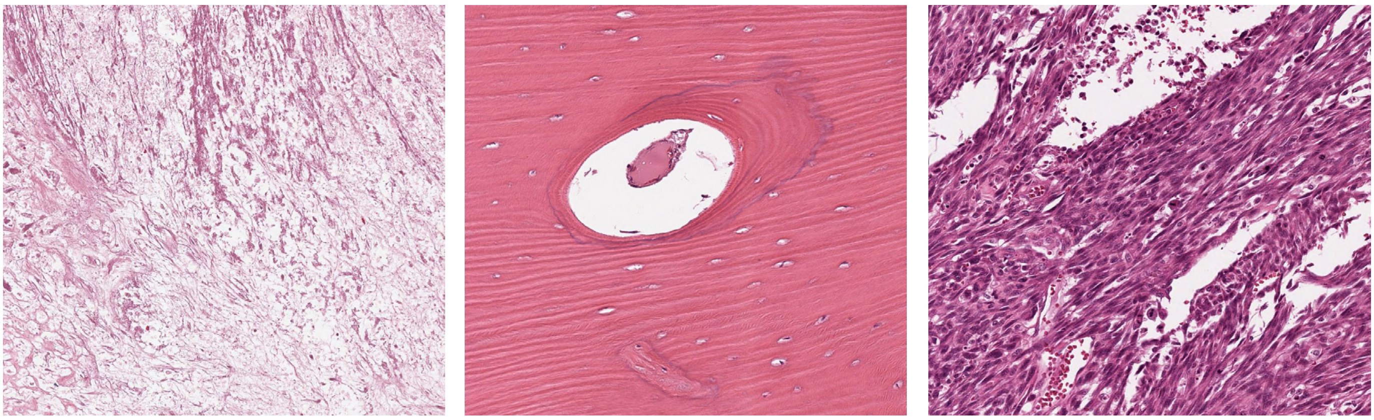
Dataset

Leavy et al.27 curated a collection of histology photos of osteosarcomas stained with haematoxylin and eosin (H&E). This staining technique is commonly used in cancer research, where tissues appear pink and nuclei are dyed blue in the images. Currently, pathologists manually examine stained slides to detect cancer, and tumours, and assess their size, which is a time-consuming process[28].

In the case of osteosarcoma, both normal and tumour cells are stained blue, but they can be differentiated based on their shapes. Normal cells exhibit round and regular shapes, while irregular shapes indicate tumour cells, which can vary in type. The histological variability within osteosarcoma is significantly high, making it challenging to apply methods designed for other tumour types[28].

The dataset used in this study was collected by a team of clinical scientists from the University of Texas Southwestern Medical Center in Dallas. It consists of archived samples from 50 patients who received treatment at Children's Medical Center in Dallas between 1995 and 2015. Four patients were selected by pathologists to represent a variety of tumour specimens obtained through surgical excision. Two pathologists collaborated to annotate the images, with each pathologist annotating a specific set of photos. Therefore, each image in the collection has only one annotation. The dataset includes 1144 photos with a resolution of 10X and a size of 1024 X 1024. The images are categorized into three classes: Viable Tumor, Non-viable Tumor, and Non-Tumor. Figure 2 provides an example of images from these three classes:

Figure 2



(a) Non-viable Tumor. (b) Non-Tumor. (c) Viable Tumor.

Figure 2. Types of Osteosarcoma Images- A. Non-viable Tumor, B. Non-Tumor, C. Viable Tumor.

Overview of Applied Models

EfficientNet

The Google Brain Team developed EfficientNet, a powerful transfer learning (TL) model, by studying network scaling. They found that adjusting the depth, width, and resolution of a neural network can enhance its performance. By scaling the neural network, they created deep learning models that surpass the effectiveness and accuracy of previously used convolutional neural networks (CNNs). EfficientNet has demonstrated impressive capabilities in large-scale visual recognition tasks, particularly in the ImageNet dataset. It employs a composite scaling technique, where the network depth corresponds to the number of layers, the width relates to the number of filters in a convolutional layer, and the resolution is determined by the

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input image's dimensions. Notably, EfficientNet has shown promising results even when used with the transfer learning approach, extending its utility beyond the ImageNet dataset. There are eight versions of the model available, each offering different parameters and levels of accuracy. In this study, EfficientNetB7 is applied for tumour detection[7].

ResNet

In 2016, the deep residual network, also known as ResNet, was introduced as a solution to address the challenges associated with training deep learning models. ResNet was designed to overcome the limitations of shallow networks and the time-consuming nature of training. This complex model offers a shortcut approach that does not compromise performance. It enables more efficient network training by reducing computational calculations. ResNet achieves this by skipping ReLu-activated layers and batch normalization. Additionally, it utilizes Stochastic Gradient Descent (SGD) to optimize weights and parameters. ResNet has gained a reputation for its superior feature extraction capabilities, surpassing the performance of other models in this aspect12.

InceptionResNet

InceptionResNet is a widely utilized transfer learning model that combines the strengths of two highly effective models, Inception and ResNet. Trained on the ImageNet dataset, this model employs batch normalization instead of convolutional layer summation. To prevent overfitting, dropout layers randomly set input units to 0 during the training phase. The model utilizes flattening techniques to convert data into one-dimensional arrays before passing it to subsequent layers. A similar process is applied to output data to create a feature vector. For classification, the model incorporates a fully connected layer, and a "binary cross-entropy" loss function is employed with a batch size of 329.

NasNet

Google developed the Neural Architecture Search Network-Large (NASNet-Large) as a powerful solution to the challenge of finding the optimal Convolutional Neural Network (CNN) architecture. By treating this task as a Reinforcement Learning (RL) problem, NASNet-Large leverages its computational power and technical expertise. Unlike other models focused on tensor decomposition or quantization, NASNet introduces a machine-assisted approach to designing deep neural networks without relying on predefined architectures. The process involves training a super-network, analyzing sampled networks, and training the selected architecture. The search cycle's success is measured by the accuracy achieved on the given dataset. NASNet-Large has demonstrated exceptional performance in the ImageNet competition, achieving state-of-the-art results. Notably, the model has a fixed image input size of 331 x 331 pixels13.

Evaluation Criteria

The output is assessed on 5 criteria: accuracy, loss, precision, recall and AUC. Outputs are divided into 4 categories: True Positive (TP), True Negative (TN), False Positive (FP), and False Negative (FN). The categories are explained in Table 1:

Table 1. Explanation of TP, TN, FP, and FN.

I/O	Output Positive	Output Negative
Input Positive	True Positive (TP)	False Positive (FP)
Input Negative	False Negative (FN)	True Negative (TN)

Accuracy

Expressed by percentage, accuracy measures how well the predicted outcome matches the actual outcome. It is calculated by multiplying the total number of possible outcomes by the number of true positive and true negative outcomes:

Accuracy = (TP + FN) / (TP + TF + FP + FN)

Precision

Precision is calculated by dividing the true positive by the total of true and false positives. It indicates the degree to which projected outcomes agree with one another.

Precision = TP / (TP + FP)

Recall

By dividing the total number of true positives by the sum of true positives and false negatives, Recall is calculated:

Recall = TP / (TP + FN)

The Adam Optimizer was used for the experiment. The name 'Adam' was derived from 'Adaptive Moment Estimation'. Because of its property that combines the efficiency of AdaGrad for sparse gradients with the ability of RMSProp to perform effectively in non-stationary environments, Adam has become one of the most popular optimizers used for deep learning24.

RMSEValue

RMSE (Root Mean Squared Error) is a valuable evaluation criterion for assessing the predictive accuracy of models. It quantifies the average magnitude of prediction errors by calculating the square root of the mean of squared differences between predicted and actual values. RMSE provides a clearer understanding of the model's performance and the dispersion of errors, helping researchers to gauge the reliability of predictions and identify areas for improvement. Lower RMSE values indicate better agreement between model predictions and ground truth, making it a useful tool for comparing and selecting models with superior accuracy and precision.

Other parameters used in this study for the selected models are mentioned in Table 2:

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Table 2. Parameters used to build the selected models.

Parameter	Value
Batch size	32
Epochs	50
Runtime	GPU
Platform	Google Colab
Loss	Categorical Loss Entropy

RESULTS

Based on the information presented in Tables 3 and 4, several observations and conclusions can be made. Firstly, the loss values for the validation set are consistently higher than those for the training set across all models. Notably, NasNetLarge exhibits the largest disparity between these two values, with the validation loss being 12.48 times greater than the training loss. On the other hand, ResNet50 demonstrates the lowest loss values and the smallest difference between them, with the validation loss being greater than or equal to 1.52 times the training loss. Regarding precision and recall, all models perform equally for both the training and validation sets, except for ResNet50. InceptionResNetV2 achieves the highest precision and recall values for the validation set (0.8658), while NasNetLarge achieves the highest values for the training set (0.9759). EfficientNetB7, on the other hand, displays the lowest precision and recall values for both sets among the four models.

In terms of accuracy, NasNetLarge achieves the highest accuracy on the training set (98.80%), followed by InceptionRes NetV2 (98.30%), ResNet50 (89.16%), and EfficientNetB7 (71.69%). However, for the validation set, InceptionResNetV2 exhibits the highest accuracy (93.29%), followed by NasNetLarge (90.91%), ResNet50 (89.83%), and EfficientNetB7 (62.77%).

Incorporating RMSE analysis allowed us to gain further insights into the models' predictive accuracy. EfficientNetB7 displayed the highest RMSE value (19.39025), indicating notable discrepancies between its predicted and actual tumour classes. In contrast, InceptionResNetV2 demonstrated the lowest RMSE (3.04962), suggesting a higher level of agreement between its predictions and ground truth. NasNetLarge and ResNet50 fell in between, with RMSE values of 6.78716 and 0.20255, respectively. These RMSE insights provide a valuable perspective on the models' performance and can guide future improvements in their predictive capabilities.

Based on these results, it can be concluded that the comprehensive analysis of transfer learning models for osteosarcoma tumour detection reveals that InceptionResNetV2 and NasNetLarge emerge as the most effective options for this critical medical application. The models' performance analysis, combined with the RMSE evaluation, offers a holistic understanding of their strengths and limitations. The reported findings contribute to the growing body of knowledge in medical image analysis and tumour detection, potentially guiding researchers in selecting suitable models and optimizing their performance for more accurate osteosarcoma detection.

Table 3. Performance of the selected models for Osteosarcoma Detection.

Model	Loss	Accuracy	Precision	Recall	AUC
For Training Set					
EfficientNetB7	40.6399	71.69%	0.4337	.4337	0.6309
InceptionResNetV2	0.5040	98.30%	0.9660	0.9660	0.9830
NasNetLarge	1.3211	98.80%	0.9759	0.9759	0.9839
ResNet50	0.8564	89.16%	0.7895	0.7722	0.9324
For Validation Set					
EfficientNetB7	83.9986	62.77%	0.2554	.2554	0.5036
InceptionResNetV2	7.3212	93.29%	0.8658	0.8658	0.9195
NasNetLarge	16.4955	90.91%	0.8182	0.8182	0.8886
ResNet50	1.3083	89.83%	0.7991	0.7992	0.9250

Table 4. RMSE Value of the models used for the Osteosarcoma Tumor Detection.

Model	RMSEValue
EfficientNetB7	19.39025
InceptionResNetV2	3.04962
NasNetLarge	6.78716
ResNet50	0.20255

DATA AVAILABILITY

The data and materials involved in this study have been collected from publicly available sources. The dataset analysed during the current study is available in The Cancer Imaging Archive repository, https://doi.org/10.7937/TCIA.AXH3-T579 Codes can be provided upon request.

Author Contributions Statement

All the mentioned authors have made substantial contributions to the conception of the work, revised it critically for important intellectual content and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All the mentioned authors have approved the version to be published. All authors contributed to the study's conception and design. All authors read and approved the final manuscript.

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- Ethics approval: This article does not contain any studies with human participants or animals performed by any of the authors. No human or animal was involved in the process. The researchers worked only with publicly available medical imaging data.

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