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Predicting and Staging Hepatocellular Carcinoma from Contrast CT Scans

Md Zakir Hossain[1,3] Patrick Buckley[1]
Himadri Shekhar Mondal[2] Md Rakibul Hasan[3] Tom Gedeon[1,3]
[1] School of Computing, Australian National University, Canberra, Australia
[2] School of Engineering, Australian National University, Canberra, Australia
[3] School of Elec Eng, Comp and Math Sci (EECMS), Curtin University, Perth, Australia
{zakir.hossain, patrick.buckley, himadrishekhar.mondal}@anu.edu.au;
{zakir.hossain1, Rakibul.Hasan, tom.gedeon}@curtin.edu.au

***Abstract*—Hepatocellular carcinoma (HCC) is a common and deadly form of liver cancer for which early detection and staging can be integral to patient survival. Medical imaging is an usual method of diagnosis, either using contrast Computed Tomography (CT) scans or Magnetic Resonance Imaging (MRI) scans. We introduce a new deep learning model that aims to take advantage of the information in two different stages of contrast CT scans to predict the presence and severity of HCC tumours in the images. Our model is trained and tested on a dataset of 307 labelled dual image input slices. On testing, the model achieves an accuracy of 96.8% and a sensitivity of 87.8%. These results indicate that using a dual image input of contrast CT scans provides a significant boost in performance to the model. Such a model prove to be a valuable tool to assist doctors in the diagnosis and staging of HCC, saving them time in the manual examination of scans. Implementation is publicly available at https://github.com/ZakirANU/CNN4LiverCancer.**

***Index Terms*—Convolutional Neural Networks, Hepatocellular Carcinoma, Cancer Detection, Machine Learning**

I. Introduction

Hepatocellular carcinoma (HCC) is the most common form of liver cancer, making up 75-85% of liver cancer cases. It is the sixth most common form of cancer and the third highest cause of death among cancers globally [1]. Early detection and staging of HCC are often critical for patient survival outcomes. Cancer staging is a process for diagnosis of the severity and nature of a cancerous tumour. At its simplest, the staging can be split into four categories: Stage I, Stage II, Stage III, and Stage IV, with higher stages representing a more severe and developed cancer [2].

A. Staging and Detection of Hepatocellular Carcinoma

There are several methods of staging and detection considered appropriate by the medical community for the diagnosis of HCC [3] [4]. Serum tests involve full blood tests to measure hormone levels and blood cell counts, which may indicate the presence of cancer [5]. This is usually a preliminary test for detection and requires further testing if the result indicates cancer is present. The test also detects specific chemicals produced by tumours called tumour markers. Another staging method is biopsy analysis and histopathology. This involves taking a small sample of the tumour and using it to determine the severity of the present cancer. Histopathology is the analysis of images of this sample. This procedure is very invasive when applied to HCC, requiring surgery to obtain a sample from the liver. Biopsy analysis is not useful for detection and is only applicable to staging the cancer.

The last and most popular method for detection and staging is the analysis of medical images. Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are the two imaging methods used for this. While MRI is considered to be the slightly more informative scan, MRI scanners are far less available than CT scanners [6]. Analysis of these scans can be time-consuming, and occasionally, doctors can make mistakes [7]. A tool that can automatically detect the presence of cancer in a scan and make predictions on its severity would save doctors valuable time and hopefully reduce errors made.

B. Applications of Convolutional Neural Networks

Deep learning models are a form of supervised learning in which a model is trained on a labelled dataset. The model is able to learn the data patterns that correlate with the different labels. Convolutional neural networks (CNNs) are a form of deep learning which is usually applied to image datasets. CNNs specialise in learning based on the location and positions of data. This is very useful for visual data, where information comes from not just one pixel but the surrounding pixels as well. CNNs can be applied to medical images to predict the presence and severity of cancer based on learnt visual patterns. Computed Axial Tomography (CAT), or in short Computed Tomography (CT), scans with contrast are one of the two most common methods of performing cancer imaging [8].

C. Purpose and Usage of Contrast CT Scans

Contrast CT scans are one of the main methods that radiologists use to identify and stage HCC tumours [9]. The varying contrasts assist in differentiating the cancer from benign tumours such as Hemangioma or Hepatocellular adenoma. The density of a cancerous tumour tends to be similar to healthy liver tissue making it difficult to distinguish them on non-contrast scans. Thus, contrast scans enable tumours to be more

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easily identified. To perform a contrast CT scan, the patient must have a slightly radioactive contrast agent injected into their bloodstream. The scan then has two phases: the arterial phase and the portal venous phase. The arterial phase occurs while the contrast agent is in the arteries and causes the arteries and tissue supplied blood by the arteries to become very bright. The portal venous phase occurs while the contrast agent is in the veins and causes a similar but less intense brightness in the veins and the tissue they supply blood to.

The differing levels of blood supply between cancerous tumours and liver tissue make the tumours stand out much more in contrast scans than in non-contrast scans. HCC tumours typically receive all of their blood supply from the hepatic artery. As such, the arterial phase will cause the tumour to appear brighter than the surrounding tissue. However, the portal venous phase should show the tumour as washed out and slightly darker than the surrounding liver tissue. Occasionally (particularly in later-stage tumours), the arterial phase will not show a tumour at all, while the portal venous phase will show the tumour as a particularly dark region. This tends to occur when the tumour is larger or when there are multiple medium-sized tumours. Figure 1 depicts four sample images containing cancer from the dataset. It exemplifies the visual patterns seen in contrast CT scans that relate to HCC.

Analysis of medical imaging is a popular application for computer vision and deep learning models. Many have achieved great success in building models for analysing histopathological images [10] [11]. However, these images require invasive procedures to be performed on the patient. There have also been several models applied to CT scans that have managed to outperform radiologists. Despite a small abundance of machine learning models being applied to tumour detection [12] [13] [14], there are scopes to reduce the gaps between radiology detection methods and computer vision methods. There have been very few models which make use of the contrast differences in multi-phase contrast CT scans. Our major contributions include, *(1)* New input for the application of CNNs to CT scans for cancer detection by using a dual image that learns contrast patterns and *(2)* A novel model with high-performance when predicting the presence and severity of cancer in contrast CT scans.

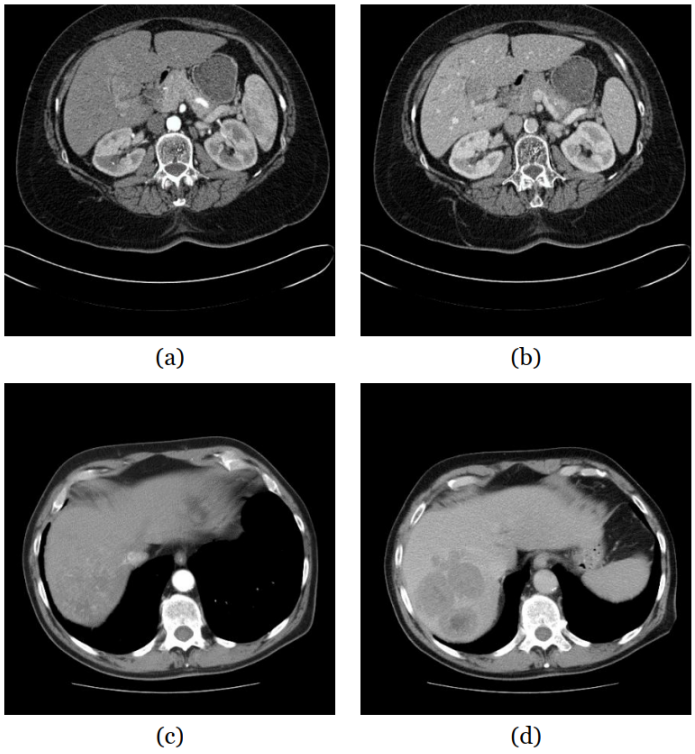

Fig. 1. Appearance of early and late-stage HCC in contrast CT scans. *(a) Arterial scan:* The region slightly left of the centre top of the image shows a region slightly brighter than its surroundings. *(b) Portal venous scan:* The same region in the arterial scan is shown to be slightly washed out, indicating a likely tumour. *(c) Arterial scan:* There are no clear signs indicating the presence of a cancerous tumour. The bright spot has no matching washout. *(d) Portal venous scan:* The particularly dark regions in the bottom left of the image indicate multiple cancerous tumours.

II. Methodology

The model we have created makes its cancer predictions using CAT or CT scans with contrast as its input. Every single input to the model is comprised of two image slices: an arterial CAT scan and a portal venous CAT scan. The model will then determine, based on the inputs, whether there is a cancerous tumour present in the given images. If the model detects a tumour, it will also predict the severity of that tumour into two groups of early-stage or late-stage cancer.

A. Advantages of CT and MRI Scans

We elected to train our model on contrast CT scans due to the logistical advantages over MRI and performance advantages over non-contrast CT scans. There have been previous cancer prediction models that have made use of MRI datasets and non-contrast CT datasets [15] [16]. While MRI is considered to be a generally more informative scan than CT, MRI is also much costlier to perform. Additionally, MRI machines are much less widespread in their accessibility. CT scans are easier to perform but tend to make it more difficult for radiologists to identify cancers. Our model aims to solve this issue and match or exceed the performance of existing models using contrast CT scans.

One of the major drawbacks of contrast CT scans, however, is that they unnecessarily expose the patient to radiation at levels higher than X-rays [3]. Such radiation exposure may result in side effects and very rarely in severe complications, particularly for children. These risks are uncommon, and as such, contrast CT scans remain a popular medical imaging technique. After some consideration, we decided that this prediction model should use contrast CT scans as input, with the aim of making it more widely applicable while maintaining a high-performance level.

B. Model Inputs

We trained our CNN on individual slices of both arterial phase and portal phase CT scans overlaid as two features. CNNs are highly reliant on local information. By overlaying

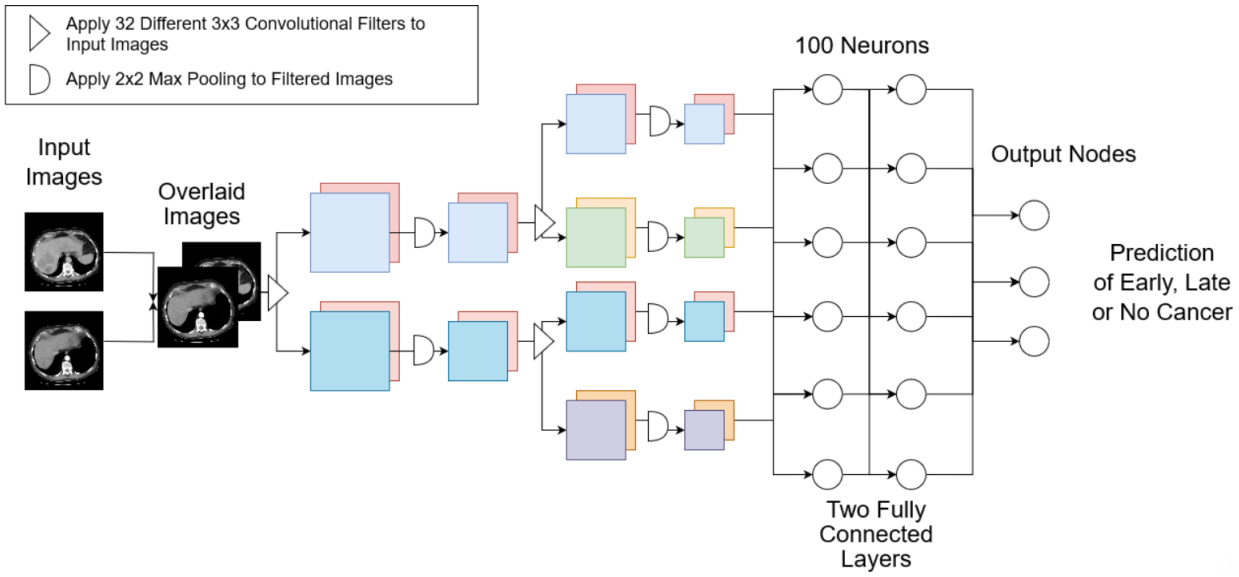

Fig. 2. Our Convolutional Neural Network Architecture for predicting cancer.

the two images, the model is able to use not only the information from the surrounding pixels for one image in the convolutional layers but also the pixel information from the second image in the same relative location in the scan. In this way, the model is able to detect the pattern of bright spots in the first image and washed-out spots in the second image. As mentioned previously, this is a very common pattern that radiologists look for in contrast CT scans during cancer detection. Thus, by forming the inputs as two separate contrast scans stored as features, the CNN is able to enhance its performance by understanding how the contrast differences between the images relate to the presence and severity of cancer tumours.

C. Model Architecture

The architecture we developed is a CNN, depicted in Figure 2. The architecture is designed to predict the presence and label of HCC severity analysing dual-phase contrast CT scans. The inputs are first overlaid into two feature layers to enable easier contrast detection. The first convolutional layer applies 32 different 3x3 filters to the stacked images for highly basic feature detection. The first pooling layer applies maximum pooling to detect the brightest pixel in each 2x2 of pixels. These two layers are repeated for higher-level feature detection. Finally, two dense 100-node layers are applied to make sense of the detected features and allow the model to make its predictions.

We labelled each of the dataset's input slices based on the presence and severity of cancer in the single images. A *'0'* indicates Stage 1 or Stage 2 cancer, a *1* indicates Stage 3 or Stage 4, and a *'2'* indicates no cancer present, in the image, at all. This is to avoid the scenario where a patient is labelled as having cancer, but the image slice being shown to the model does not have this cancer present. Such a scenario inhibits the CNN's learning process as the model associates a perfectly healthy image with a cancer label. Due to the nature of the scans, where the cancer only appears on a small minority of the images in each scan, the dataset is rather heavily skewed, and most input slices have a label indicating no cancer. In the dataset of 307 input slices, 227 of these are labelled as having no cancer present. The skewed dataset means that when judging the performance of the model, the precision and specificity should also be considered.

Before feeding the contrast CT scans into the model, several pre-processing steps are applied to ensure that the input data are suitable for the CNN. First, the CT scan slices are standardized to ensure uniformity across the dataset, as the scans came from different medical facilities with varying acquisition protocols and machine settings. Each input consisted of two slices: one from the arterial phase and one from the venous phase, which are overlaid as feature layers to enable the model to learn contrast differences. The images are resized to a fixed resolution to maintain consistency in input dimensions, and pixel values are normalized to fall within a specific range (between 0 and 1) to prevent large variations in pixel intensity.

D. Dataset

The dataset we used comes from The Cancer Imaging Archive (TCIA)[1], which is a subset of data from the Cancer Genome Atlas [17]. The specific collection we used is TCGA-LIHC, which contains the medical scans for 97 different cancer patients. Each patient has a unique set of scans made up of MRI, CT and contrast CT scans from various angles. The data has been gathered from many patients from all over the world using different scanner modalities, scanner manufacturers and acquisition protocols. As a result, the dataset is highly heterogeneous. The Cancer Genome Atlas

[1]https://www.cancerimagingarchive.net

also provides demographic and medical information about each patient. Of this information, only the tumour staging was used for labelling the severity of cancer in the dataset. In the final dataset, 307 pairs of image slices from contrast CT scans among patients with varying degrees of cancer severity are selected. Each of these image slice pairs is then labelled based on the presence and severity of cancer in that particular slice.

E. Differences in Early and Late-Stage HCC

The labels that depict the severity of the cancer are split into two categories: early-stage cancer and late-stage cancer. Stages 1 and 2 are classified as early-stage cancer, and stages 3 and 4 are classified as late-stage cancer. While cancer is in its earlier stages, it is often feasible to remove the cancerous tumour through surgical procedures. Alternatively, the cancerous liver may be replaced through a liver transplant. However, in later stages, the cancer is much more widespread, extending beyond the liver, and often, it becomes more difficult to separate from the tissue. Due to these complications, treatment options become more difficult. Usually, for these later-stage cancers, the only options are radiation therapy and chemotherapy to destroy the cancerous cells. The prediction labels in the model attempt to match diagnosis with the treatment option outcomes with this split.

F. Performance Evaluation

Accuracy measures the overall correctness of a model's predictions and calculated as the ratio of the number of correct predictions (true positives and true negatives) to the total number of predictions (Eq. 1). Accuracy provides an overall assessment of a model's performance but can be misleading in the presence of imbalanced datasets like the dataset we used. We, therefore, evaluated our model using specificity (Eq. 2), sensitivity (Eq. 3) and F1 score (Eq. 4), in addition to the accuracy[2]. The evaluations provide a balanced measure by taking both false positives and false negatives into account. These metrics are commonly used in classification tasks, especially when the dataset is imbalanced or when both false positives and false negatives are of concern [18].

$$Accuracy = \frac{TP + TN}{TP + FP + TN + FN} \tag{1}$$

$$Specificity = \frac{TN}{TN + FN} \tag{2}$$

$$Sensitivity = \frac{TP}{TP + FN} \tag{3}$$

$$F1\ Score = \frac{2 \times Specificity \times Sensitivity}{Specificity + Sensitivity} \tag{4}$$

Before reporting average performance, we use K-fold cross-validation approach where K = 5. It involves dividing the data into K equally sized subsets or folds. The model is trained K times, each time using (K-1) folds for training and the remaining fold for validation. The K-fold cross-validation helps address the issue of over-fitting and provides a more robust estimate of the model's performance [18].

[2]TP = True Positive, TN = True Negative, FP = False Positive, and FN = False Negative

III. Results and Discussion

From the results shown in Figure 3 in the form of confusion matrices, our model achieves remarkable performance. In testing, the average accuracy across the five folds is 96.8%, as seen in Table 1. This is indicative of generally high performance for classifying an image. However, for a model such as this one, sensitivity is a crucial consideration. Cancers going undetected may have serious adverse implications for patients. Thus, our model's performance on images that do contain cancer is a necessary consideration on which to base its success. Our model does achieve relatively high sensitivity, with an average of 87.8% across the 5 folds. For inputs in which cancer is detected, the model was able to differentiate between early-stage and late-stage cancer correctly with 100% in every fold. The performance in cancer staging is very promising and demonstrates our model has a good understanding of the visual differences between early and late-stage cancer.

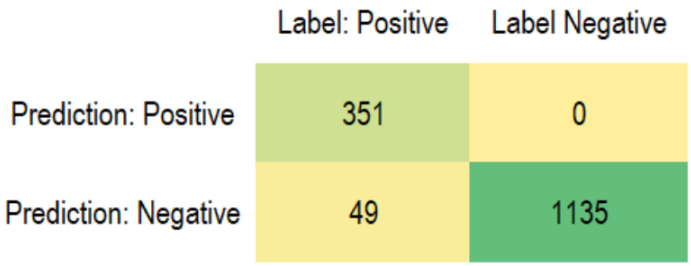

Fig. 3. Confusion matrix depicting aggregated results from five folds.

TABLE I
Performance (in %) of each fold

Fold	Accuracy	Specificity	Sensitivity	F1 Score
1	93.4	91.9	75.0	85.7
2	98.0	97.4	92.5	96.1
3	98.0	97.4	92.5	96.1
4	96.7	95.8	87.5	93.3
5	97.7	97.0	91.3	95.4
Average	96.8	96.0	87.8	93.3

These values indicate that the model is not quite fit to replace the expertise of radiologists. However, it would be satisfactory as an assistive tool to save doctors time in examining many scans and providing a preemptive indication of cancer severity. The performance of our model is made more impressive by the heterogeneity of the dataset on which it has been trained and tested. The obtained results indicate that the model has been made highly resilient to variations in the scan. The variations in the dataset result from different scanning modalities, scanning manufacturers, and scanning protocols. This is encouraging for the model's applicability to real-world uses as the model is able to interpret many different styles of scan. Our model's performance varies quite heavily based on

TABLE II
EFFECT OF NETWORK ELEMENT ON PERFORMANCE (IN %)

Removed Element	Accuracy	Specificity	Sensitivity	F1 Score
Veinous Scans	94.1	92.7	77.5	87.3
Arterial Scans	94.5	93.0	78.8	88.1
Convolutional and Pooling Layer	73.9	73.9	0.0	0.0
Fully Connected Layer	95.4	94.2	82.5	90.4

the class of scan it is given. It performs well differentiating images containing early-stage cancers from images containing late-stage cancers and images of healthy livers, with an average accuracy of 96.8% when classifying these images. This indicates that the model has gained a strong understanding of the contrast patterns and shapes that relate to early-stage cancer. Additionally, the model perfectly classifies every image of a healthy liver, resulting in no false negatives. On average, the model has some issues with differentiating images of late-stage cancers from images of healthy livers. The accuracy for these images is only 53.8%, with all misclassifications being predictions of no cancer presence. Late-stage cancers tend to be much more varied in both contrast and shape when shown in scans, providing additional challenges when applying pattern recognition for prediction. This challenge can be enhanced by a relatively smaller sample size of these types of images. This may be a potential cause for the reduced performance levels with this class of images.

Beyond automation, the proposed CNN model offers significant advantages over traditional diagnostic methods for detecting and staging HCC. First, the model significantly enhances diagnostic accuracy by leveraging contrast differences between arterial and venous phase CT scans, a technique that helps differentiate cancerous tumors from healthy tissue. By combining and analyzing these dual-phase images, the model can detect subtle patterns that may be missed by human observers, particularly in early-stage tumors. In addition, the model reduces the time required for diagnosis, offering quick and consistent results compared to the labor-intensive and variable manual interpretations by radiologists.

There are a few limitations of our experiment. The most significant of these is the limited amount of data samples with severe cancer present, which affected its performance on these types of cancers. There may potentially be visual patterns associated with later-stage cancer that the model has not learnt sufficiently due to the limited amount of training data. Additionally, the CNN's multi-image input requirement relies on the images from the two scans to align relatively well. Misaligned scans may drastically reduce the performance of the model.

A. Ablation Study

We performed tests on the neural network to determine how influential various elements of the architecture. The tested element was removed before being rerun against the data to observe the impact on performance, and the results are depicted in Table 2. The first experiment involved removing the dual feature input from the model and instead feeding a single image into the model. This was done for both types of images to ensure that one image type was not more informative for the model's predictions. The results show that both image inputs provide a very similar level of performance for the model. However, in this experiment, the single image inputs resulted in a 2-2.5% decline in accuracy and, more significantly, a 6-9% reduction in sensitivity, indicating that the dual-input feature architecture does provide a significant boost in the neural network's prediction capabilities.

The next experiment involved removing one of the convolutional layers and pooling layers from the architecture. This resulted in the neural network collapsing and simply predicting no cancer on every given input. This is unsurprising as removing these layers inhibits the model's ability to perform higher-level feature detection in images, which is necessary for identifying cancer tumours. The final experiment involved removing one of the fully connected layers involved with making the final prediction. The result of this was a slight drop in accuracy by 1.4% while sensitivity fell by 5.3%. This indicates that the fully connected layers do allow the model to achieve more accurate predictions.

B. Comparative Analysis

While there have been no other models tested on the TCGA-LIHC dataset, there are several similar models which have comparable performance, as shown in Table 3. Chen et al. [13] and Lin et al. [11] use a dataset of histopathologic images in their models. They achieve good accuracy of 95.3% and 91.4%, respectively, but the downside is such images require surgery on the patient to obtain. Krishan et al. [16] achieves 87.0% accuracy when distinguishing between malignant and benign tumours.

TABLE III
COMPARISON OF PERFORMANCE WITH SIMILAR STUDIES.

Study	Data Used	Accuracy (%)
This Study	**Contrast CT Scans (Liver)**	**96.8**
Chen et al. [13]	Histopathologic Images (Liver)	95.3
Ali et al. [19]	Quantitative/Qualitative (Liver)	90.3
Zhongrui et al. [12]	Tumor images (various)	94.0
Krishan et al. [16]	CT Scans (Liver)	87.0
Lin et al. [11]	Histopathologic Images (Liver)	91.4

There are some other approaches to cancer prediction that have achieved good performance. Ali et al. [19] use the quantitative and qualitative features of a patient to predict the presence of cancer and achieve an accuracy of 90.3%. Such a performance indicates that the usage of contrast CT scans as input may provide boosts in performance. Among these,

our model achieves the highest accuracy for predicting the presence of HCC.

Although, the focus of our study was developing a CNN model for HCC detection, future work will explore its integration into clinical workflows. Automating the detection and staging of HCC can reduce the time and effort required by radiologists, particularly in high-volume settings. However, collaboration with clinical professionals will be essential to ensure the model is designed for practical use. In addition, our future research will focus on improving the model's interpretability through visualization techniques, ensuring it can serve as a decision-support tool for assisting radiologists.

We also focused on developing and applying a CNN to contrast CT scans where dual-phase images from both the arterial and venous phases are overlaid as features. This enables the model to detect patterns associated with cancer presence and severity based on contrast variations. While the dataset includes 307 image pairs from 97 patients but they represent a diverse set of scanner modalities and patient conditions. Future work will focus on addressing the dataset limitations by exploring advanced data augmentation techniques and benchmarking the model against state-of-the-art methods to provide a more comprehensive evaluation.

IV. Conclusion

Hepatocellular carcinoma (HCC) is a deadly disease that affects many people around the world. The only method of diagnosis which avoids surgical procedures is normally a time-consuming analysis of medical imaging. This paper develops a deep learning model, convolutional neural network (CNN), which is capable of automatically predicting the presence and severity of HCC in contrast CT scans with high accuracy and specificity. The model emulates the methods by which radiologists detect cancers using the contrast differences between various phases of the scan. The results we have shown in this paper through this model are encouraging and indicate that this methodology does have the potential to assist radiologists in identifying cancers.

In addition to HCC staging, our future work aims to upgrade the model for predicting biomarkers related to cancer [14] or other diseases [20] and evaluating other cancer types, like leukemia [21]. Further, the dataset we used contains MRI and CT scans which were left unused in this model. However, we intend to create a multi-modal model which is able to use a variety of scan information to make its predictions.

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