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Developing a novel computer-aided diagnostic technique based on deep learning and CT images for early HCC diagnosis

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Purpose

Hepatocellular carcinoma (HCC) constitutes a prominent global health challenge. According to the American Association for the Study of Liver Diseases (AASLD) guideline HCC can be diagnosed by imaging examination. However, it shows that contrast-enhanced CT has limited accuracy in the diagnosis of HCC, particularly, small-size HCC lesions (≤ 20 mm) are the most difficult to identify with CT demonstrating sensitivity = 64% [1]. An Artificial Intelligence (AI) algorithm that can analyze liver CT images and localize HCC lesions is valuable for patients at risk of HCC. Recent studies have presented promising outcomes regarding the application of AI algorithms in HCC diagnosis; However, the efficacy in localizing small-sized HCC lesions in CT images remains uncertain, and there is a need for improvement in reducing the false-positive rate [2-4].
We studied a novel computer-aided diagnostic technique, based on deep learning (DL) to assist radiologists in increasing the diagnosis accuracy on Contrast-enhanced multiphasic CT scans.

Methods and materials

Methods

The proposed DL model combines a specifically designed convolutional 3D classifier and a state-of-the-art 3D detector (3D-RetinaUnet). It leverages the arterial and portal venous phases of CT scans as input and provides the locations of HCC lesions as output.

Our global workflow (Figure 1) has two main branches, the one with Median in-house developed Multiscale Autoencoders [5,6] and the one with the Retina 3D-Unet branch. Each branch processes the arterial and portal phases together and proposes a set of 3D bounding boxes as candidates for the HCC lesions. These boxes are merged using the Weighted box Fusion off-the-shelf algorithm.

Data preprocessing is necessary before proceeding:

- Phases soft registration with DEEDS to put the two volumes in the same geometric coordinates: the voxel in the arterial phase corresponds to the voxel in the portal phase.
- Resampling of the volumes to the same spacing dimension (1mm x 0.68mm x 0.68mm).
- Liver segmentation to restrict the work area of the autoencoders and filter out-of-the-liver false positives for the Retina 3D-Unet. Liver segmentation is done using the combined multi-dimensional approach that is based on the adapted 3D SegResNet-VAE and 2D LinkResnet34 models.

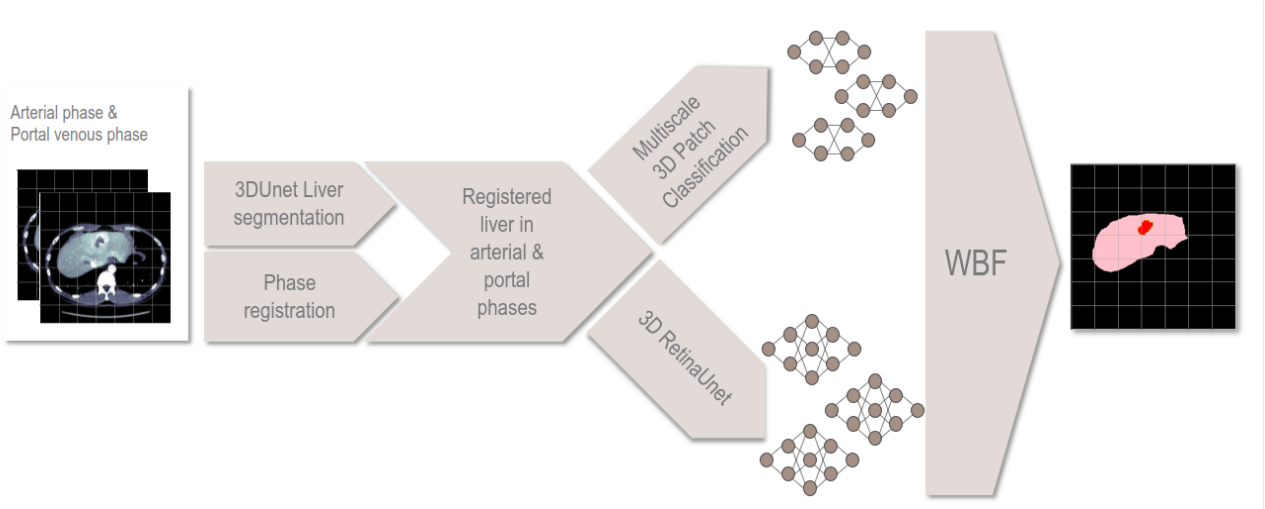

Figure 1: HCC detection global workflow.

Our autoencoders are trained on small volumes from arterial and portal venous phases stacked together. These volumes are taken either from the background liver (i.e., background BG class) or the HCC lesions annotated by the radiologists (i.e., HCC class). The classification is learnt from the bottleneck feature jointly with the reconstruction, the idea being that autoencoders will help to find out the features that help to discriminate between the two classes.

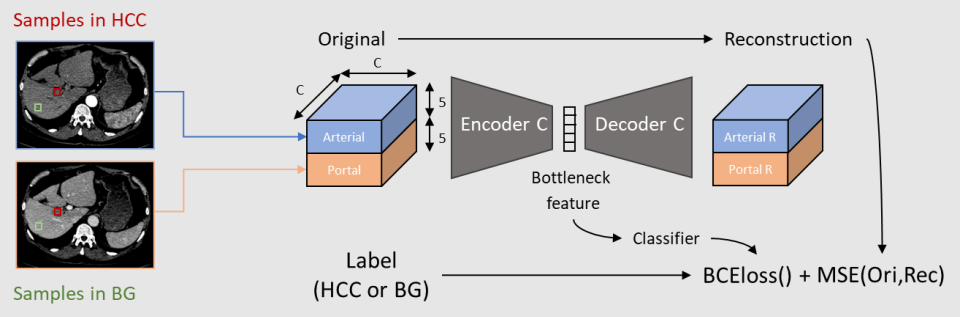

Figure 2: Autoencoders learning workflow

RetinaUnet:

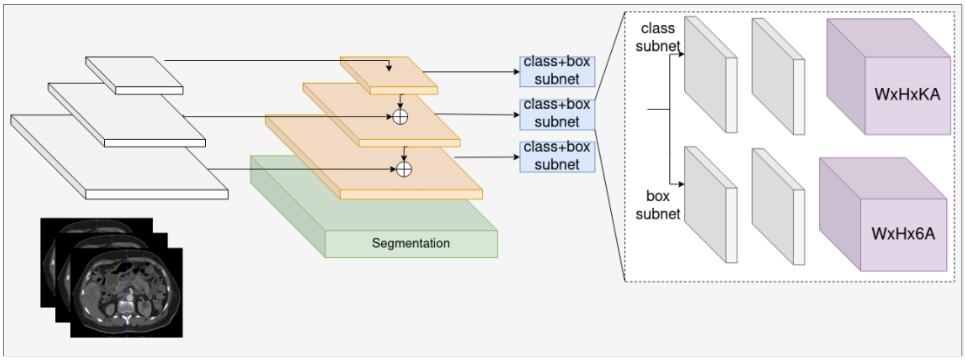

Figure 3: Retina 3D-Unet learning workflow

The RetinaUnet3D [7] model undergoes training with 3D patches resampled to a consistent size and spacing. This model consists of a feature extraction backbone and applies a multiscale Feature Pyramid Network, mirroring the structure of the symmetric U-Net. Each feature layer contributes to class classification and box regression. The lowest feature layer is employed to train with the segmentation mask, introducing an additional loss alongside the original box regression and classification losses. To address the potential issue of multiple detections on the same lesions when using different models, the Weighted Box Fusion algorithm [8] is employed to consolidate predictions.

Materials

The dataset is part of the Phenotyping Liver Cancer Registry (NCT04681274), which collects multiphase CT, and clinical data of liver cancer patients from 3 French sites (La Pitié-Salpêtrière, Beaujon and Paul Brousse). 884 patients were selected for this study based on inclusion criteria:

- Patients with a histopathologically confirmed diagnosis of HCC
- Patients underwent contrast-enhanced multiphase CT imaging, including both arterial phase and portal venous phase, and slice thickness ≤ 3 mm;
- Patients had not received liver cancer treatment prior to CT imaging.

Enrolled patients' characteristics and CT scans	
Patient's age at CT scans	68.7 ± 12.2 years old
Gender	Male 80% Female 20%
Etiologies (Some patients have more than one liver background disease)	Alcohol Use 37% Hepatitis B 18% Hepatitis C 26% Nonalcoholic Steatohepatitis 19%, Hemochromatosis 3% Others 12%
Metavir (Fibrosis) stage	F0 11% F1 8% F2 11%, F3 15% F4 (cirrhosis) 41%

	Unknown 14%
CT Manufacturers	GE 57.2% Philips 33.7% Siemens 8% Toshiba and others 1.1%

The training dataset is comprised of 705 CT scans with 1128 HCC lesions (778 lesions histopathologically confirmed, 350 lesions diagnosed by radiologists). The test dataset consisted of 179 CT scans in which 181 HCC lesions were histopathologically confirmed, including 12 HCC lesions smaller than 20 mm, 42 of size between 20 and 30 mm, 66 of size between 30 and 50 mm. Three expert radiologists collaboratively annotate HCC lesions on each patient's CT images, guided by patient information on background liver disease and lesion histopathological characteristics. The process involved one radiologist localizing HCC lesions, a second radiologist adding bounding boxes to the lesions on each CT slice, and a third radiologist reviewing, adjusting and confirming the outputs.
More precise distributions are given for training and test set in Figure 4.

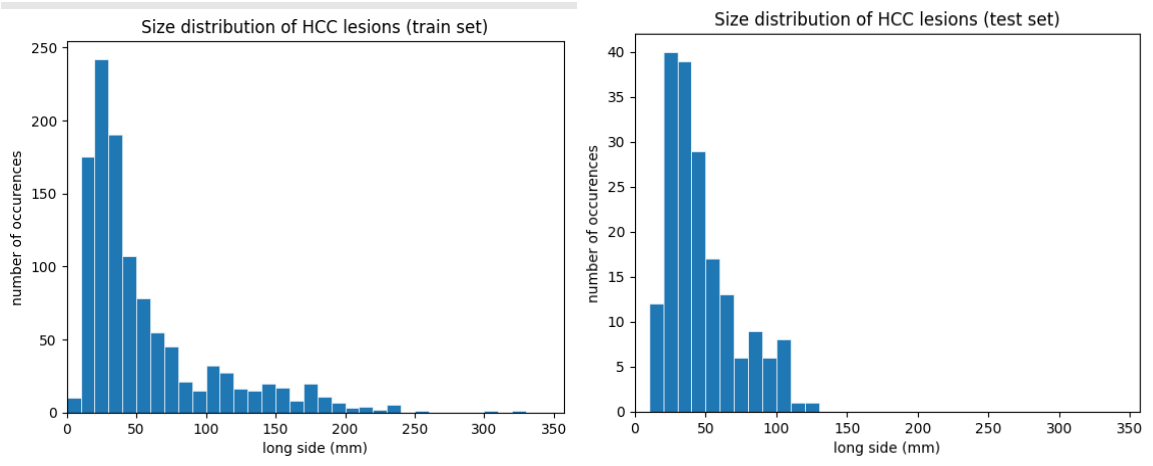

Figure 4: Distribution of the lesion sizes reported in the histopathological reports for training and test set.

Results

Figure 6 displays the FROC curves for 3D Intersection over Union (IoU). The IoU is depicted in figure 5, it measures how good the localization of the detection. A corrected detection is recognized when the IoU between the detection box and the ground truth box is higher than a certain threshold (0.1, 0.2 and 0.3 in our case). IoU=1.0 means a perfect match between the detection and the radiologists' annotation.

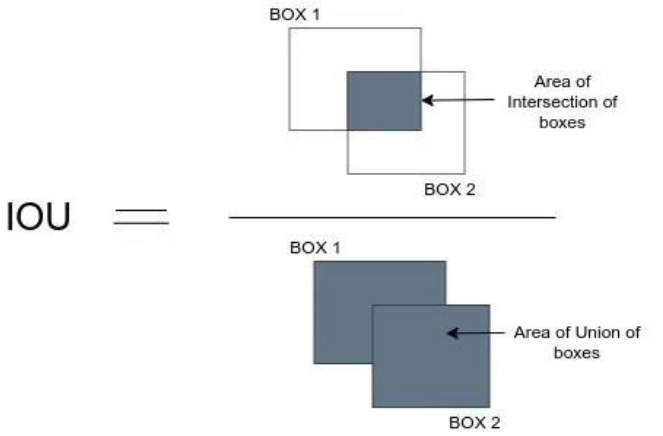

Figure 5: IoU computation method (2D toy example). BOX 1 is the bounding box for a detection, BOX 2 is the bounding box for the annotation of a lesion.

At 3.0 false positive per scan (FP/s) we have sensitivity of 0.945, 0.928, 0.900, respectively for an IoU= 0.1, 0.2 and 0.3.

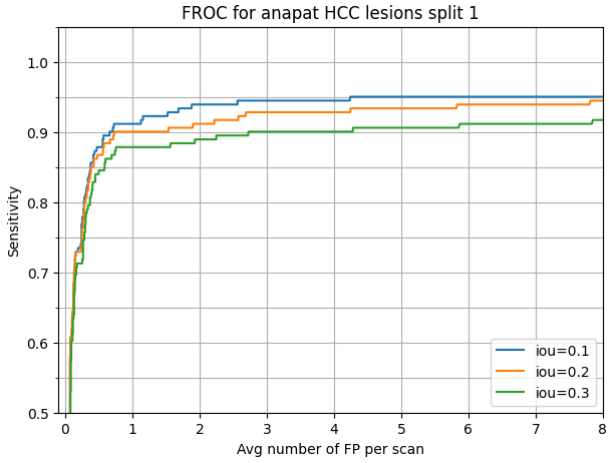

Figure 6: FROC of the Proposed Model Localizing All Histopathologically-proved HCC Lesions In Test Dataset

At 3.0 FP/s, the detection result and sensitivity (%) stratified by lesion size (S) and IoU threshold are presented in Figure 7:

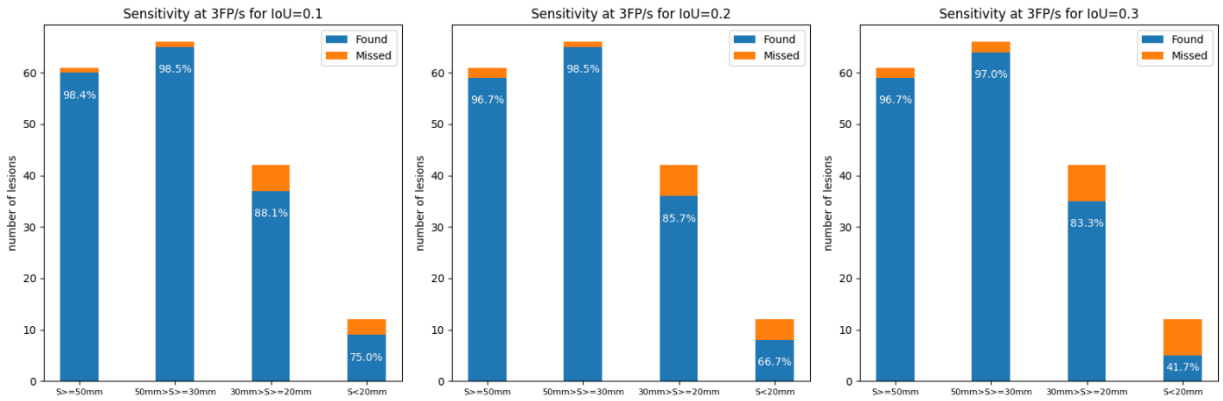

Figure 7: Sensitivity stratified by lesion size (S) at 3.0 FP/s at IoU = [0.1,0.2,0.3]

An example of our HCC detection pipeline is presented in Figure 8, where a small-size HCC is correctly detected.

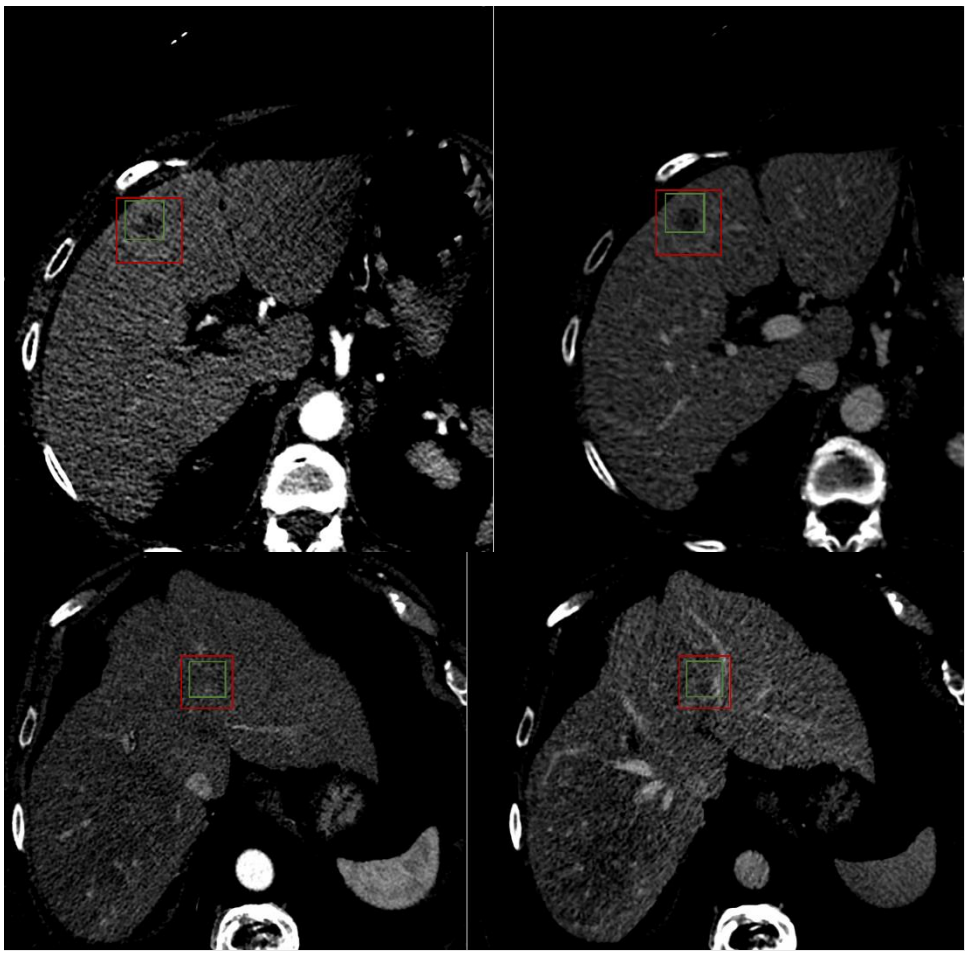

Figure 8: HCC detection examples (2 patients on 2 lines, arterial phase on the left, portal phase on the right), the ground truth boxes are in green, the detection boxes are in red.

Conclusion

Our DL model could potentially increase HCC diagnosis accuracy compared to state of the art (Sensitivity of 64% for diagnosing small HCCs [1]). The next step is to refine our DL model further and augment the training dataset with more at-risk patients with benign and malignant liver nodules and masses. Our goal is to develop an end-to-end Computer-Aided Detection and Computer-Aided Diagnosis (CADe/CADx) that will improve the diagnosis accuracy for HCC, particularly for localizing small-size HCCs on CT images. In this paper, we achieved this objective with a sensitivity of 75% at IoU = 0.1 using our HCC detection pipeline based on dual phases CT scans. This initiative aims to contribute to the refinement of clinical practices in HCC identification and diagnosis.

Personal information and conflict of interest

To be added when uploading poster.

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