Supplementary Information

Focal Liver Lesion Diagnosis with Deep Learning and Multistage CT Imaging

Supplementary Tables

Supplementary Table 1: Basic information of all radiologist.

Name	Time as Radiologists	Tile	Working Institution
Zheying Zhan	3	Resident Physician	Quzhou Hospital Affiliated to Wenzhou Medical University, Quzhou People's Hospital
Shufeng Xu	10	Attending Physician	
Guozheng Zhang	14	Associate Chief Physician	

Supplementary Table 2. The decision of three radiologists in testing cohort.

	Benign [right/all (correct)]	Malignant [right/all (correct)]	HCC [right/all (correct)]	ICC [right/all (correct)]	MET [right/all (correct)]	FNH [right/all (correct)]	HEM [right/all (correct)]	CYST [right/all (correct)]
LiLNet	94/104 (90.4%)	107/117 (91.5%)	32/37 (86.5%)	32/40 (80.0%)	33/40 (82.5%)	30/34 (88.2%)	33/35 (94.3%)	33/35 (94.3%)
Junior	87/104 (83.7%)	104/117 (88.9%)	25/37 (67.5%)	21/40 (52.5%)	31/40 (77.7%)	21/34 (61.8%)	29/35 (82.9%)	32/35 (91.4%)
Middle	89/104 (85.6%)	103/117 (88.0%)	21/37 (56.7%)	32/40 (80.0%)	22/40 (55.0%)	23/34 (67.6%)	29/35 (82.8%)	33/35 (94.3%)
Senior	92/104 (88.5%)	104/117 (88.9%)	19/37 (51.4%)	31/40 (77.5%)	24/40 (60.0%)	25/34 (73.5%)	31/35 (88.6%)	33/35 (94.3%)

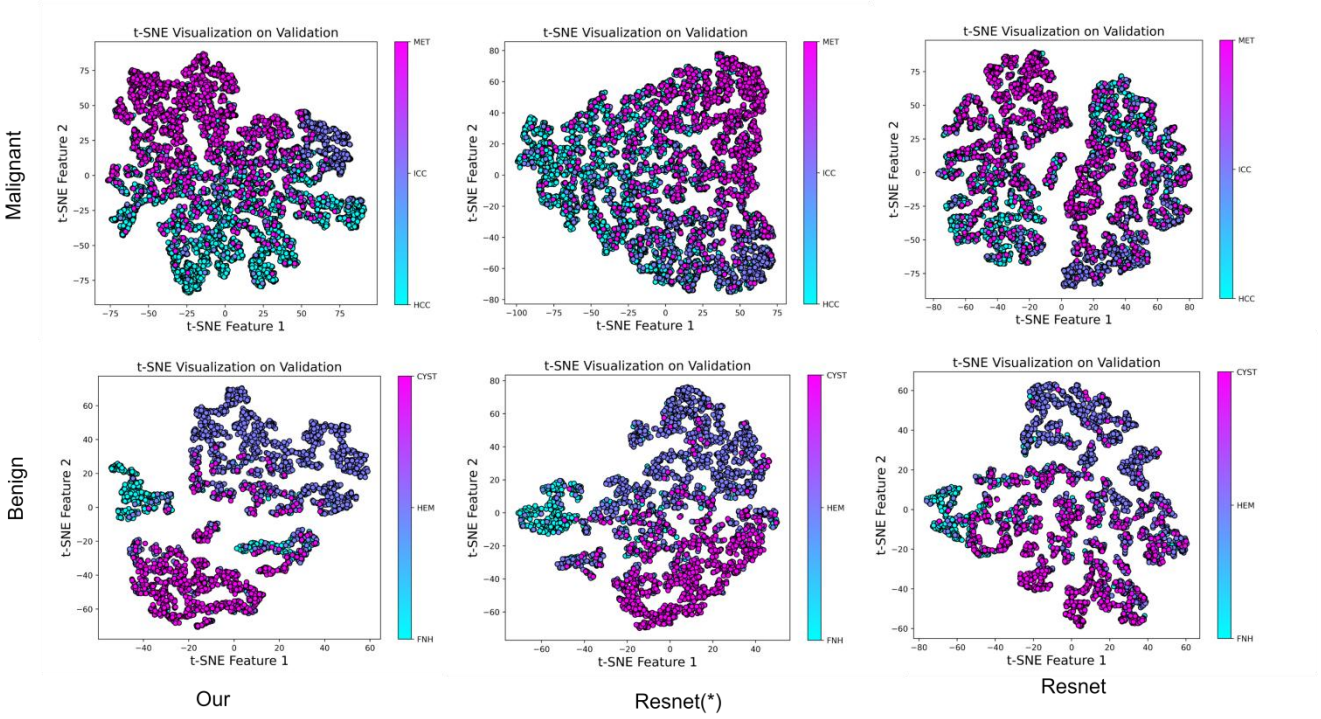
Supplementary Table 3. The decision Fleiss Kappa. In our data analysis, we employed two-sided t-test without adjustments for multiple comparisons.

Classification	Fleiss Kappa	Standard Error	Z Value	P Value	95% CI
Fleiss kappa test between three radiologists					
Benign VS. Malignant	0.782	0.039	20.128	0.000	0.781-0.782
Malignant	0.687	0.024	28.836	0.000	0.687-0.687
Benign Classification	0.815	0.024	33.399	0.000	0.815-0.815
Fleiss kappa test between AI model and high-level expert group (junior and senior radiologists)					
Benign VS. Malignant	0.806	0.039	20.760	0.000	0.806-0.807
Malignant	0.711	0.024	29.601	0.000	0.711-0.712
Benign Classification	0.848	0.024	35.041	0.000	0.848-0.848

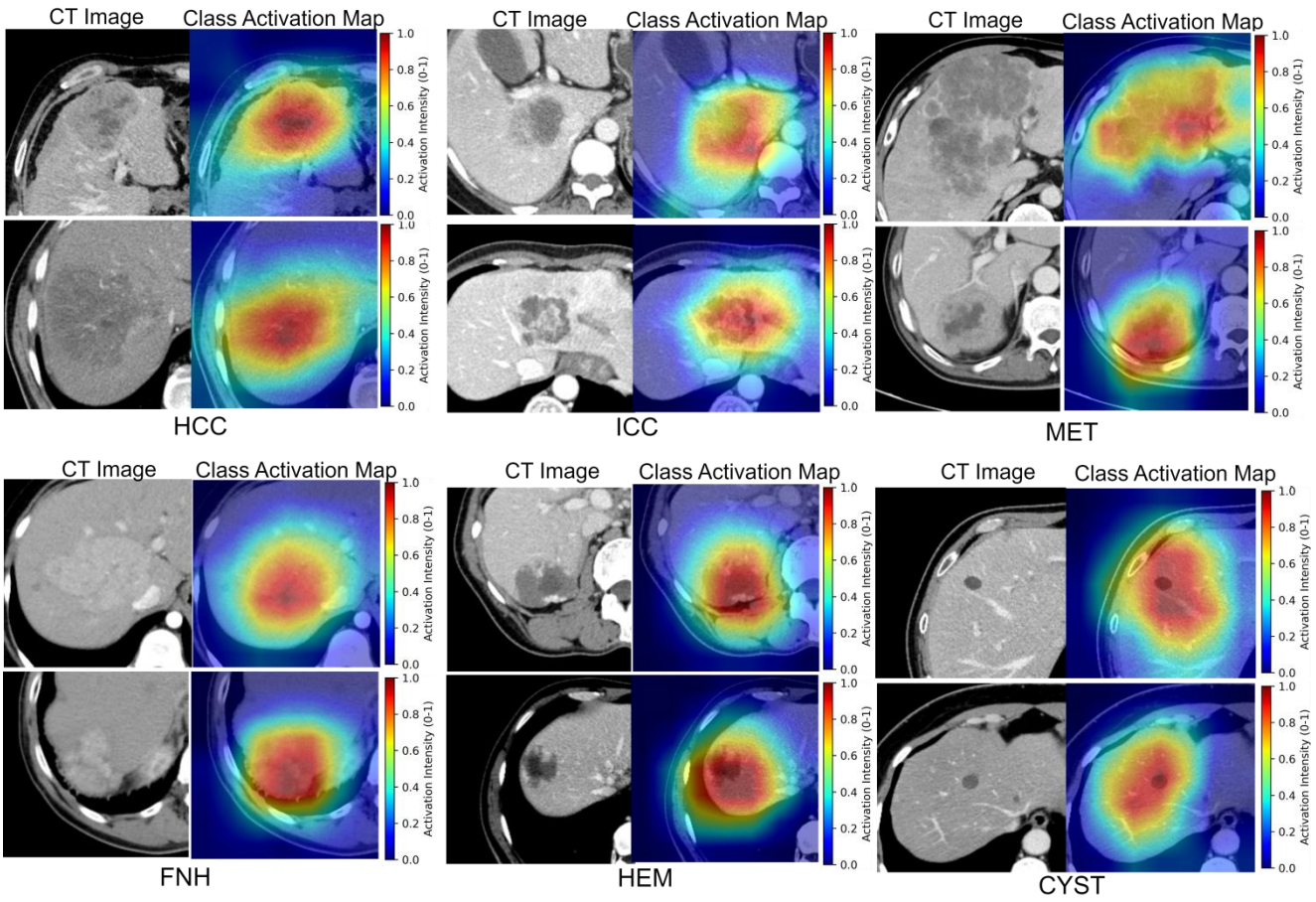
Supplementary Table 4. CT image acquisition conditions.

Parameters	GE Healthcare	Siemens Healthcare	Philips Healthcare	United Imaging
kV	100-120	100-120	100-120	100-120
mAs	NA	210	109	180
mA	430	NA	NA	NA
Pitch	0.992	1.0	1.386	0.993
Rotation time	0.5 s/rot	0.5 s/rot	0.5 s/rot	0.5 s/rot
Reconstruction of thick slices (CT)	5mm	5mm	5mm	5mm
Reconstruction of thick slices (AP)	1-3mm	1-3mm	1-3mm	1-3mm
Reconstruction of thick slices (PVP)	1-3mm	1-3mm	1-3mm	1-3mm

Supplementary Figures



Supplementary Fig. 1: Visual comparison of t-SNE between the proposed model (Our), loaded with pre-trained ResNet50 (Resent(*)) and the standard ResNet50 (Resent) on the Henan validation set. HCC: hepatocellular carcinoma; ICC: intrahepatic cholangiocarcinoma; MET: metastatic tumors; FNH: focal nodular hyperplasia; HEM=hemangioma; CYST=cysts.



HCC/hcc=hepatocellular carcinoma; ICC/icc=intrahepatic cholangiocarcinoma; MET/met=metastatic tumors; FNH/fnh=focal nodular hyperplasia; HEM/hem=hemangioma; CYST/cyst=cysts.

Supplementary Fig. 2: Visualization of the class activation map generated by the last convolution layer. Red denotes higher attention values, and the color blue denotes lower values. HCC: hepatocellular carcinoma; ICC: intrahepatic cholangiocarcinoma; MET: metastatic tumors; FNH: focal nodular hyperplasia; HEM=hemangioma; CYST=cysts.

Supplementary Methods

Fleiss Kappa test

We performed a Fleiss Kappa test on three evaluators, including junior, mid-level, and senior radiologists, to assess their diagnoses of benign and malignant tumors. The results revealed a Fleiss Kappa coefficient of 0.782, falling within the range of 0.6 to 0.8, signifying a high level of agreement among the evaluators. Similarly, when assessing malignant diagnoses, the Fleiss Kappa coefficient was 0.666, reflecting a strong degree of agreement. In contrast, for benign diagnoses, the Fleiss Kappa coefficient soared to 0.815, surpassing the 0.8 threshold, indicating a very high level of agreement among evaluators in benign tumor diagnosis. It's worth mentioning that we also conducted a Fleiss Kappa test to measure the consistency between LiLNet diagnoses and those made by experienced doctors. The results demonstrated that for both benign and malignant diagnoses, the Fleiss Kappa coefficient registered at 0.711, while for malignant diagnoses alone, the coefficient remained at 0.711. In the case of benign diagnoses, the Fleiss Kappa coefficient reached an impressive 0.848, alluding to a substantial level of agreement among evaluators. The detail information can be found in supplementary Table 3.

CT image acquisition conditions

As shown in Supplementary Table 4, CT imaging was performed by using multidetector CT scanners (Revolution, GE Healthcare, Milwaukee, USA; SOMATOM definition, Siemens Healthcare, Erlangen, Germany ； Brilliance, Philips Healthcare, Amsterdam, Netherlands; uCT780, United Imaging Healthcare, Shanghai, China). Precontrast images were first obtained before contrast agent (iodine concentration, 300-370 mg/mL; volume, 1.5－2.0 ml/kg of body weight; contrast type, iopromide injection, Bayer Pharma AG) injection. Then, the arterial phase and portal venous phase were obtained with the following parameters: For GE Healthcare, tube voltage, 100-120 kVp; tube current, 450 mA; pitch, 0.992:1; rotation speed: 0.5 s/rot; and ASIR-V: 30%. For Siemens Healthcare, tube voltage, 100-120 kVp; tube current, 210 mA; pitch, 1.0:1; rotation speed: 0.5 s/rot; and Kernel ： B30f

medium smooth. For United Imaging Healthcare, tube voltage, 100-120 kVp; tube current,150 mA; pitch, 0.987:1; rotation speed: 0.5 s/rot; and Interative reconstruction: KARL 3D. For Philips Healthcare, tube voltage, 100-120 kVp; tube current, 109 mAs; pitch,1.386:1; rotation speed: 0.27 s/rot. The arterial phase and portal venous phase were obtained at 25 s and 60-90 s after contrast injection. The slice thickness for non-contrast images were 5mm, and 1-3 mm for arterial and portal venous phase.

Comparison of methods through t-SNE

The t-Distributed Stochastic Neighbor Embedding (t-SNE) plays a crucial role in helping analysts gain insights into the data and model behavior. By visualizing the data in a lower-dimensional space, t-SNE facilitates the identification of patterns, clusters, and relationships, which can lead to better understanding and interpretation of the model's performance and predictions. As depicted in Supplementary Figure 1, we utilize t-SNE plots to visualize the feature representations learned by our model. We present the three-class benign and malignant classifications. From the plot, it's evident that relative to both pre-trained ResNet50 and ResNet50 trained from scratch, our proposed model demonstrates superior capability in separating features of different classes and expanding the feature space. This enhanced capability likely reflects our model's improved ability to segregate and abstract feature representations across different classes. Such well-separated feature representations aid the model in more accurately distinguishing between various categories, thus enhancing its performance and generalization ability in classification tasks.

Class Activation Maps

In order to visualize the impact of our method, we use Class Activation Maps (CAM) to represent the focus of the model trained by our method on the target objective. Supplementary Figure 2 presents the attention areas identified by the LiLNet model, with the red-activated regions indicating the areas that triggered the model's attention mechanisms. These regions are considered crucial for the detection of hepatic tumors compared to other areas. This visualization allowed us to gain insights into the inner workings of the model, helping us understand which regions played a significant role in predicting the status of hepatic tumors. Note that test samples are randomly selected from testing cohort and validation cohorts.

Supplementary Note 1

Hepatic lesion diagnosis system LiLNet

Instruction document

Website : http://www.liver.services

Recommended browser: Chrome Version 60 or above

Optimal display resolution: 1920 * 1080

Testing Data Download: https://github.com/yangmeiyi/Liver/tree/main/Web%20testing%20data

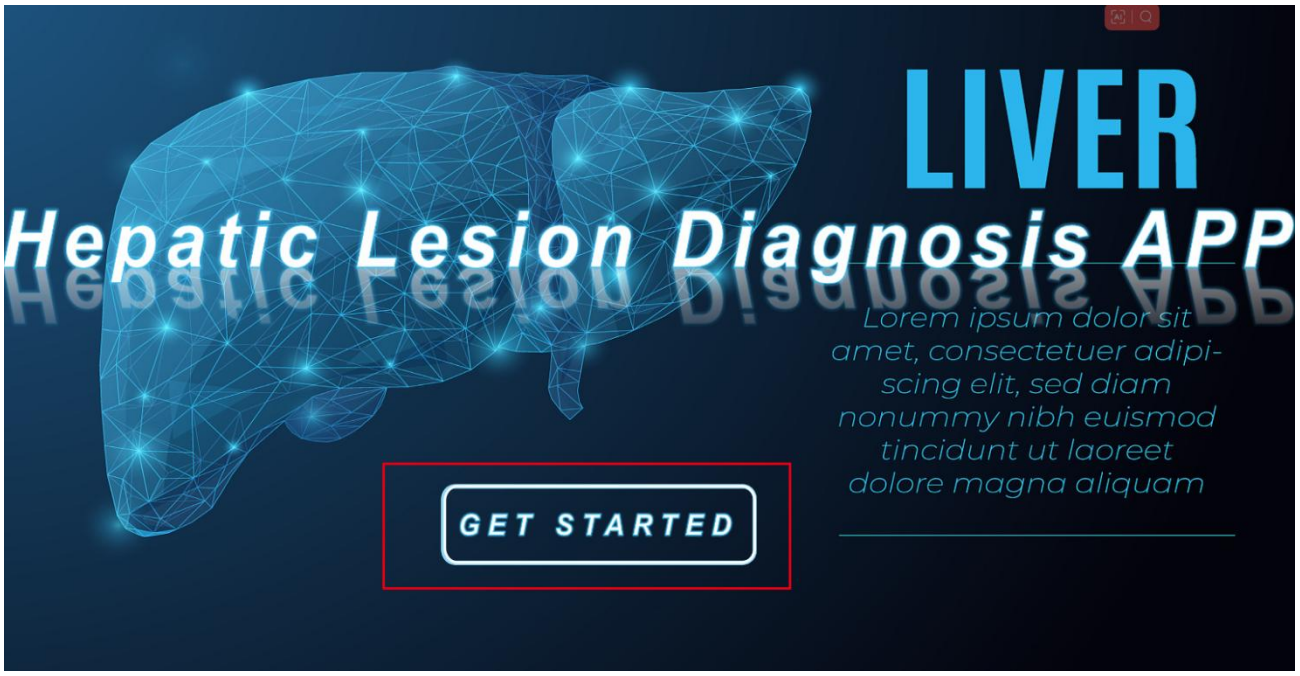
Note: If the webpage experiences a reset, please check the network

start

1. Open the following website with the Chrome browser ：

http://www.liver.services

2. Click “GET STARTED” button to start exploring the system.



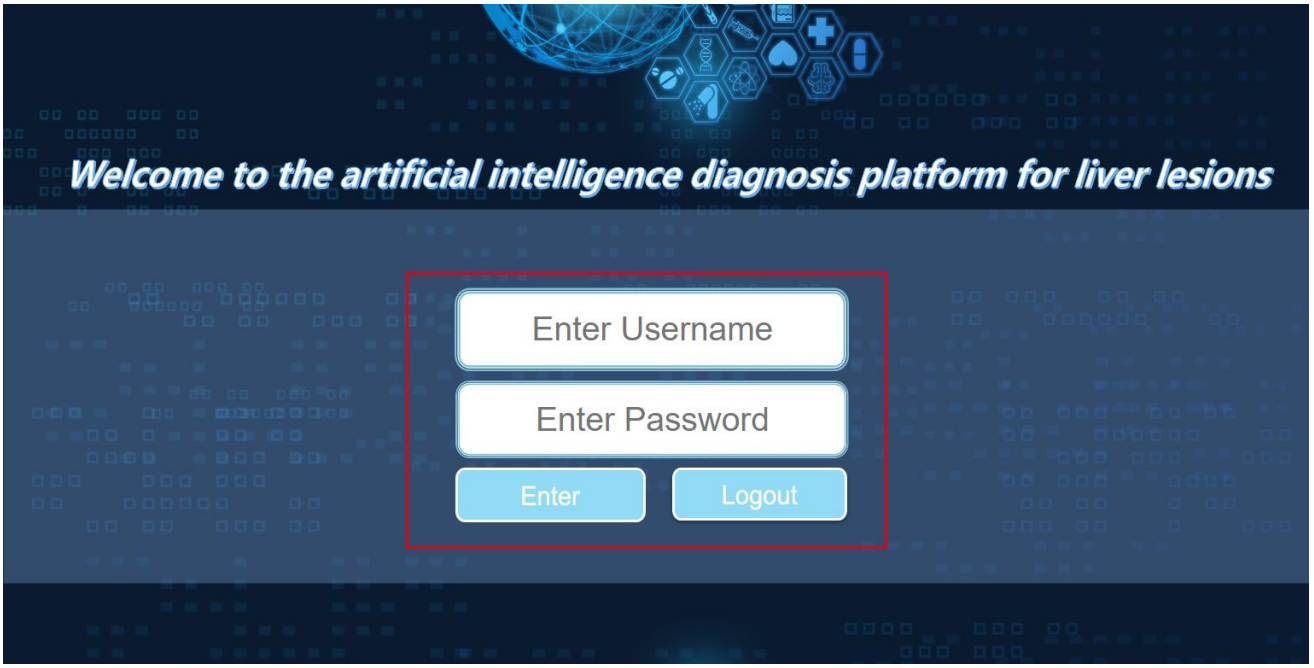
Login

1. Input your account and password following the hint in the text boxes.

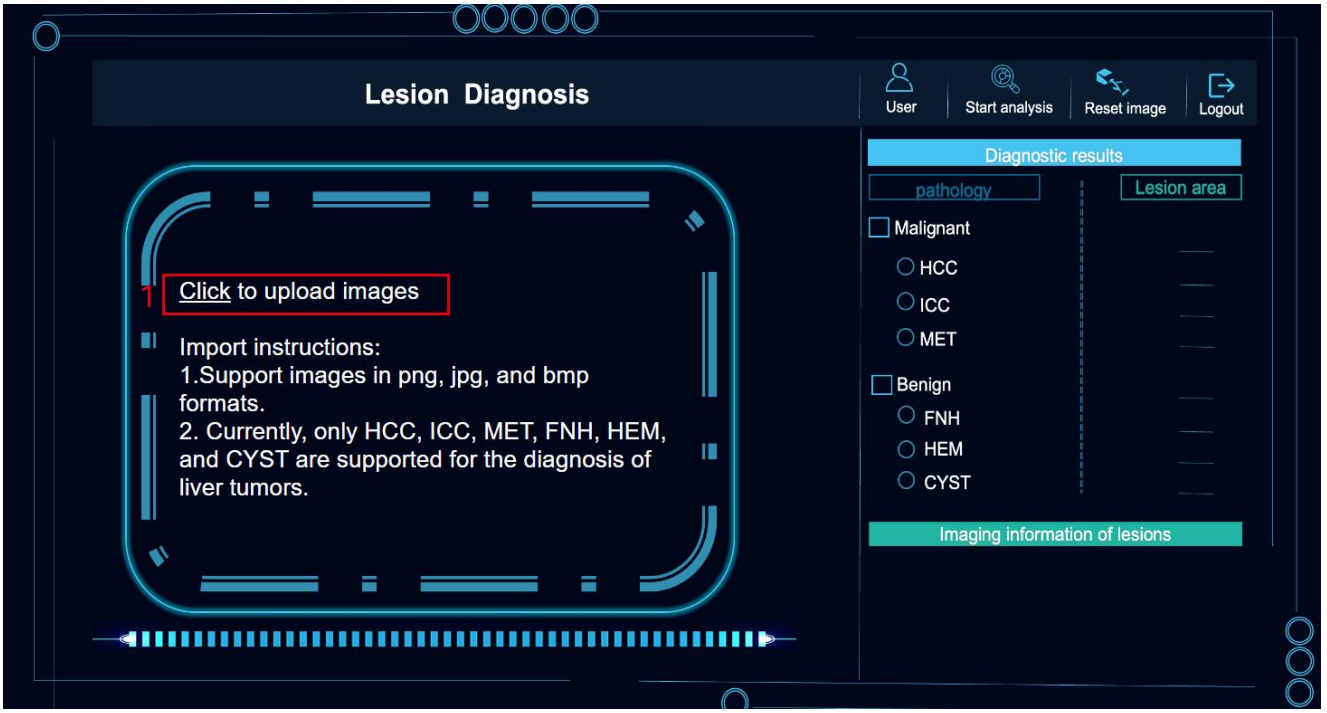
Account: reviewer

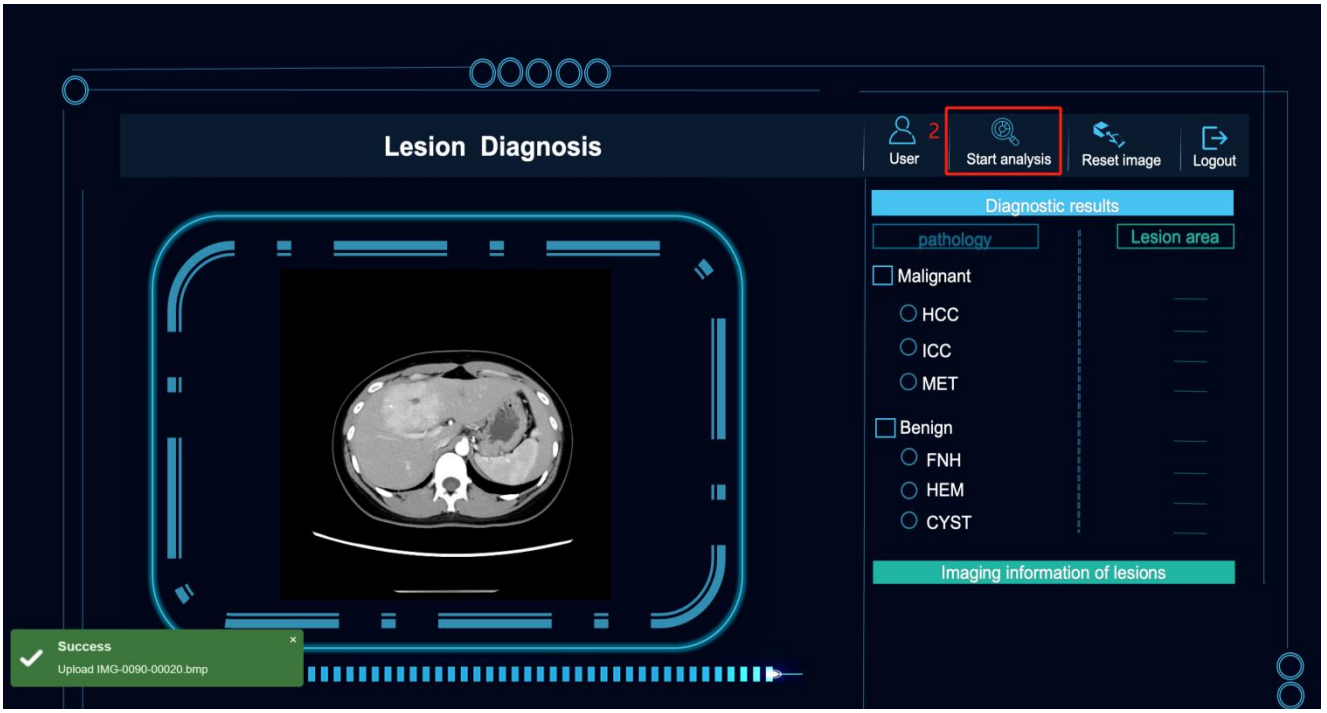
Password: reviewer

2. Click “Enter” button to login system. The page will have a pop-up displaying failure if logged-in incorrectly.


Welcome to the artificial intelligence diagnosis platform for liver lesions
Enter Username
Enter Password
Enter
Logout

Main Page


Lesion Diagnosis
User
Start analysis
Reset image
Logout
Diagnostic results
pathology
Lesion area
Malignant
HCC
ICC
MET
Benign
FNH
HEM
CYST
Imaging information of lesions
1 Click to upload images
Import instructions:
1.Support images in png, jpg, and bmp formats.
2. Currently, only HCC, ICC, MET, FNH, HEM, and CYST are supported for the diagnosis of liver tumors.

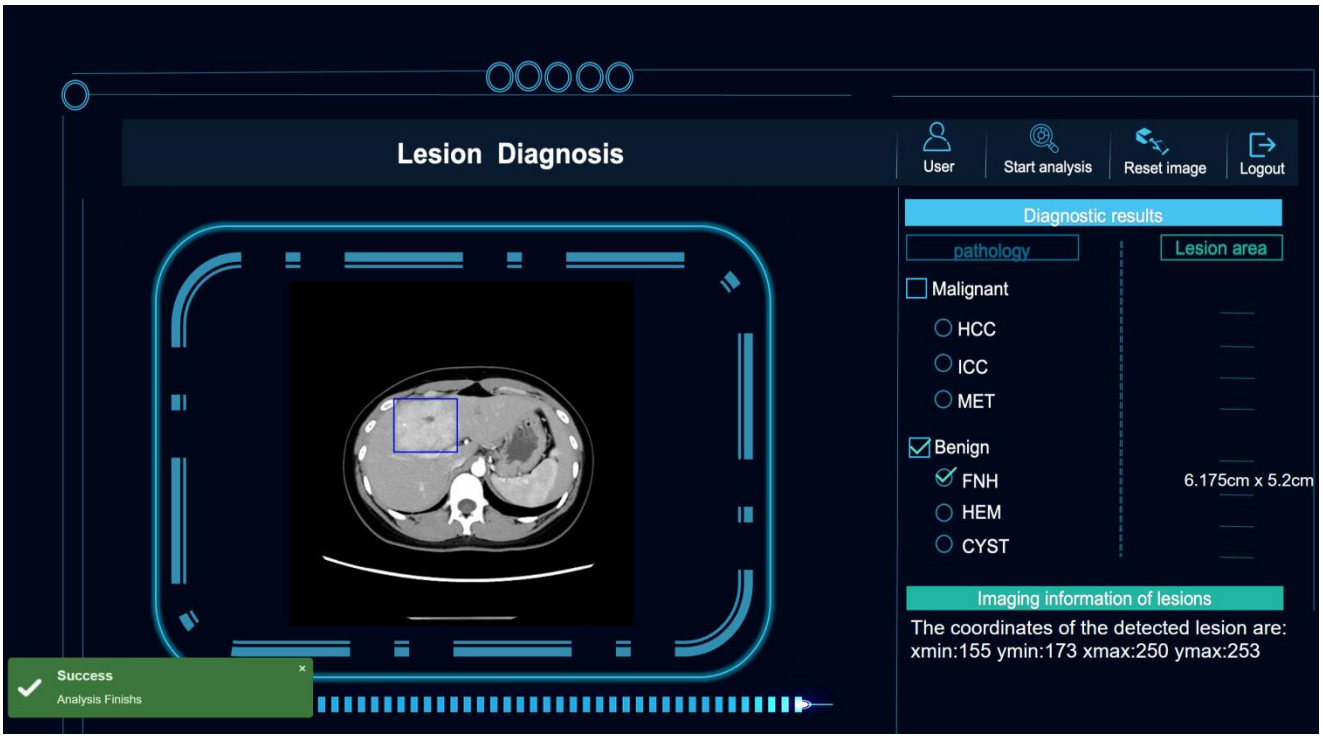


1) Click the “click” to upload an CT image.

2) After uploading the image, click the “Start analysis” button， the AI system will diagnose focal liver lesions in the image and provide the detection and classification results.

3) After a while , the AI result will be displayed in this webpage.

4) If you want to try more images, please click “Reset image” button” , and upload another image.



5）If there is no lesion in the test image, imaging information of lesions will display "None of the lesions were detected".