# Conclusion

In this thesis we successfully investigated deep learning based approaches to better characterize hepatic tumors.

After describing the potential causes that can lead to the different types of liver cancer, we motivated our choice to focus mainly on hepatocellular carcinoma (HCC).

This primary cancer type, which is the most frequent one was described through its origin, the way it is usually diagnosed, classified and treated.

The different steps transforming healthy hepatic cells to cancerous ones have been developed, along with the analysis of the physiological changes often brought throughout the process.

To better characterize the liver tumors, we have decided to rely on medical images solely, through a quantitative and objective analysis.

Regarding the modality choice, we retained the computed tomography because it currently corresponds, with MRI, to the modality providing the best quality of images for a non-invasive assessment of the disease. CT was chosen over MRI mainly because it is usually the first choice for less-specialized centers, and because it can be more easily interpreted than MRI. With our medical studies review, we showed that the use of dynamic temporal images is a prerequisite for imaging based liver cancer research.

In the clinical practice, images are usually analyzed by the experts with the naked eye, but the technological advancements allowed the creation of computer assisted diagnosis tools (CADs), where a few number of imaging features were initially used to differentiate benign and malignant lesions.

In the present work, we compared the two paradigms allowing the computer assisted analysis of medical images, either with engineered features, or thanks to deep-learning. One of the key aspects of medical images analysis being the segment, we compared the different semantic segmentation architectures, and evaluated the benefit brought by multiphase images which was most of the time neglected by previously existing studies. Then we extracted relevant features from our semantic segmentation architecture to tackle the prediction of the histological grade. Each step of our research work required imaging databases precisely annotated by experts in association with researchers to improve their applicability.

A new technology called radiomics has been developed to compute a higher number of features but it took a long time before this technology was applied to the liver, especially because of the scarcity of publicly available datasets.

We provided a detailed description of the radiomics pipeline, mainly based on a manual segmentation of the ROI, followed by the extraction of a high number of engineered quantitative features, thus being called *HCR* (Hand-Crafted Radiomics).

We presented our review, where a total of 15 *HCR* studies performed on HCC patients have been analyzed.

They were evaluated against the radiomics quality score (*RQS*) which has been developed to assess the robustness and the reproducibility of radiomics studies.

We pointed out the lack of reproducibility of the studies, with a mean *RQS* of 8.73 +/- 5.57 points out of a possible maximum value of 36 points.

Several important criteria were found as being ignored by the majority of the studies, such as a prospective design, the use of open-sourced data, the evaluation of the prediction on a validation dataset, or the extraction of features at multiple timepoints.

The emergence of deep learning has chained the way a lot of imaging related problems are comprehended.

The radiomics field has been also impacted by this novel set of algorithms, and a new paradigm called *DLR* (Deep-Learning Radiomics) has been initiated, where one or several steps of the radiomics pipeline are performed by deep learning algorithms.

We believe that the key part of the radiomics pipeline lies in the segmentation of the ROI. This step has been found to suffer from a high inter- and intra-observer variability, thus having consequences for the accuracy of the final prediction.

We reviewed the different studies using deep learning architectures to perform automatic segmentation of the liver and its tumors. We extracted the common key settings shared by the majority of them, such as the cascaded architecture or the use of a fully convolutional architecture. However, we realized the lack of studies presenting results obtained from multiphase images, which has been a key element in our work.

We performed the automatic segmentation of an internal dataset composed of 104 sparse biphasic liver slices obtained from patients suffering from HCC (images available before the injection of contrast medium: Non-Enhanced CT, and at both arterial and portal venous phases). Considering how challenging the segmentation of liver tissues is, the amount of data, and the success of such an architecture, we decided to train several specialized networks in a cascaded way.

When evaluating the performances of each specialized network, we validated the hypothesis than the use of multiphase information allows a better accuracy for each of the task than single phase based networks, with significant difference obtained for the segmentation of the liver (mean DSC of 89.9 +/- 15.6 for the multiphase network *vs* 89.5 ± 13.2 for the best single phase network) and the active part of the lesions (mean DSC of 75.5 ± 17.4 *vs* 71.6 ± 20.7).

Regarding single phase networks, the *PV* phase was the one allowing the most accurate segmentation, with significant difference vs *AR* and *NECT* for the segmentation of the parenchyma (mean DSC of 88.7 ± 15.4) , the lesion (mean DSC of 87.8 ± 9.7), and both the necrotic (mean DSC 77.8 ± 12.4) and the active (mean DSC of 71.6 ± 20.7) part of the lesion.

We validated the hypothesis that several specialized networks combined in a cascaded architecture perform better than a single network addressing all the tasks simultaneously (obtained mean slice-wise DSC of 90.5 ± 13.2 for the parenchyma, 75.8 ± 15.1 for the necrosis and 59.6 ± 22.5 for the active part of the tumor when using the cascaded architecture with the liver GT mask as input).

In a fully automatic manner (without using the liver GT mask), we were able to reach promising results regarding the size of the dataset, with a mean slice-wise DSC of 78.3 ± 22.1 for the parenchyma, 50.6 ± 24.6 for the active tumor and 68.1 ± 23.2 for the necrotic part of the tumor.

We were also able to automatically compute the necrosis rate of the tumors, with a mean error of 15.9% when compared with the experts obtained rates. This prediction is accurate enough to consider the obtained necrosis rate when evaluating the treatment outcomes.

To overcome the limited size of multiphase datasets, we define a strategy to “augment” the weakly annotated or non-annotated available datasets.

With a robust registration algorithm and our cascaded architecture where specialized networks are trained on a sufficient amount of data, we were able to perform the semantic segmentation of liver and its tumors on unseen cases.

We validated this assumption by performing the segmentation of TCIA tumors, and obtained a mean patient-wise DSC of 73.2 ± 20.6.

To predict the histological grade, we proved that features learned by our mutliphase semantic segmentation network are relevant to perform this task.

We predicted the grade for central tumor slices, and after a CV training, we correctly predicted 74% of them. When considering the patient histological grade as being the most frequent one in the central tumor slices, we were able to correctly classify 15 patients over the 18 of the dataset.

As a conclusion, our research work is the first to propose a fully automatic *DLR* pipeline with multiphase images as input. Our strategy is dedicated to small databases where the entire annotations are often not available but the same workflow can be applied for larger datasets. Our *DLR* architecture was dedicated, in this research work, to the prediction of the histological grade of HCC patients, but our strategy can be extended to other characteristics of HCC or other types of liver cancers.

Regarding the lack of publicly available datasets, we encourage the creation of an open 3D CECT dataset containing liver volumes of both healthy and diseased patients with precise and complete pathological information, and expert delineations of liver, hepatic vessels and lesions for each phase.