

# Chapter 21

## A Deep Learning Approach for Hepatocellular Carcinoma Grading

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### ABSTRACT

*Introduction and objective: Computer Aided Decision (CAD) systems based on Medical Imaging could support radiologists in grading Hepatocellular carcinoma (HCC) by means of Computed Tomography (CT) images, thus avoiding medical invasive procedures such as biopsies. The identification and characterization of Regions of Interest (ROIs) containing lesions is an important phase allowing an easier classification in two classes of HCCs. Two steps are needed for the detection of lesioned ROIs: a liver isolation in each CT slice and a lesion segmentation. Materials and methods: Materials consist in abdominal CT hepatic lesion from 18 patients subjected to liver transplant, partial hepatectomy, or US-guided needle biopsy. Several approaches are implemented to segment the region of liver and, then, detect the lesion ROI. Results: A Deep Learning approach using Convolutional Neural Network is followed for HCC grading. The obtained good results confirm the robustness of the segmentation algorithms leading to a more accurate classification.*

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## 1. INTRODUCTION

Lung/liver/stomach and bowel tumors currently account for nearly half (46%) of all cancer deaths worldwide (Torre et al., 2015). It is known that there are primary and secondary cancers depending on the organ in which the cancer arises (Bengmark & Hafström, 1969). In particular, primary liver cancers, which are constituted by pathological liver cells, rise and evolve in the liver; secondary liver cancers are defined by the cancerous areas in the liver, whose pathological cells come from a primary cancer located elsewhere in human body.

More in detail, Hepatocellular Carcinoma (HCC), Fibrolamellar carcinoma, Cholangiocarcinoma (bile duct cancer), Angiosarcoma and Hepatoblastoma (Bosch, Ribes, Díaz, & Cléries, 2004) are classified as primary liver cancers. Among them, HCC is actually the third leading cause of cancer deaths worldwide, with over 500,000 people affected by this pathology. This cancerous disease presents several interesting epidemiologic features, including dynamical behaviors; significant variations between gender, among geographic regions, racial groups and ethnic ones; however, HCC seems to be potentially preventable by means of several well-documented environmental risk factors (El-Serag & Rudolph, 2007).

Although the phenomenon of hepatocarcinogenesis is not yet completely known, there is a growing understanding on the molecular mechanisms which induce it (Farazi & DePinho, 2006). These mechanisms almost never occur in healthy liver, but the cancer risk increases sharply in response to chronic liver injury at the cirrhosis stage (Caldwell & Park, 2009). Less common causes include Wilson's disease, hereditary hemochromatosis, alpha1-antitrypsin deficiency, primary biliary cirrhosis and autoimmune hepatitis (Sanyal, Yoon, & Lencioni, 2010). A detailed understanding of epidemiologic factors and molecular mechanisms associated with HCC could ultimately improve the knowledge necessary for screening and treatment of this disease. More in detail, there are different ways in which hepatocellular carcinomas are classified, since the system to categorize HCC must incorporate stage, individual's functional status and underlying function of the liver (Waller, Deshpande, & Pysopoulos, 2015). According to the World Health Organization (WHO), HCCs can be analyzed both from a macroscopic point of view and a microscopic one; in the first case, the severity of tumor depends on the size and the presence (or absence) of liver cirrhosis; in the latter case, a histological classification includes trabecular (plate-like) tumors, pseudoglandular and acinar ones, compact and cirrhotic types (Kleihues & Sobin, 2000).

For several years, grading of HCC relied on Edmondson and Steiner system, dividing HCC into four grades - from I to IV - based on histological differentiation (Edmondson & Steiner, 1954). Grade I is the best differentiated form, consisting of small tumor cells arranged in thin trabeculae. In grade II, cells are larger and show abnormal nuclei, glandular structures and vascular invasion; in grade III, nuclei are larger (> 5 $\mu$ m) and more hyper-chromatic than grade II cells and the cytoplasm is granular and acidophilic, though less than grade II. In grade IV, tumor cells are much less differentiated with hyperchromatic nuclei and loss of trabecular pattern, invading adjacent organs (Sobin & Fleming, 1997). Most of HCCs appears as grade II or III. HCC grading is particularly important since patient's prognosis depends on HCC differentiation and its treatment typically includes liver transplantation, radiofrequency ablation (RFA) and microwave ablation, percutaneous ethanol or acetic acid ablation. As HCC tends to be untreatable when it is diagnosed at late stage, it is necessary to diagnose it in early stage by means of blood exams using liver cancer biomarkers or other specific exams.

The tests used to diagnose HCC include radiology, biopsy and AFP serology depending on the context. The most used medical imaging techniques for HCC detection are Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) and they are always required to determine the extent of disease. In

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