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# Texture analysis of baseline multiphasic hepatic computed tomography images for the prognosis of single hepatocellular carcinoma after hepatectomy: A retrospective pilot study

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ABSTRACT

*Objective:* To assess the prognostic value of texture analysis for single hepatocellular carcinomas (HCCs) after hepatectomy.
*Materials and methods:* A total of 61 HCC patients were enrolled in this retrospective study. Textural characteristics of the computed tomography (CT) images were quantified. The differences between the hepatic arterial phase and the portal venous phase were obtained (the Dif.). The receiver operating characteristic (ROC) curves were used for data screening. Cox regression analyses were performed to determine independent factors adjusted with the derived clinical and radiological variables. Model identifications were based on Akaike information criteria. Kaplan–Meier and log-rank tests were performed for overall survival (OS) and disease-free survival (DFS).
*Results:* ROC and Cox regression analyses identified five parameters. Filter 1.0 achieved the best performance, in which the Dif.Scale 1.2 was a superior indicative independent marker for OS ($p = 0.05$). Kaplan-Meier analyses further demonstrated that the Dif.Scale2.2 at filter 0 ($p = 0.001$), Dif.Scale1.2 ($p = 0.006$), Dif.Scale3.2 ($p = 0.005$) at filter 1.0, Dif.Wavelet 8 at filter 1.5 ($p < 0.001$), and corona ($p = 0.032$) were associated with OS. Moreover, Dif.Scale 2.2 at filter 0 ($p = 0.039$), Dif.Scale1.2 at filter 1.0 ($p = 0.001$), and Dif.Wavelet 8 at filter 1.5 ($p = 0.007$) were associated with DFS, while the Barcelona-Clínic Liver Cancer (BCLC) parameters showed no statistical correlation with OS ($p = 0.057$).
*Conclusions:* For patients with a single HCC treated by hepatectomy, the textural features for Gabor and Wavelet, especially the varying Dif., potentially provided prognostic information beyond traditional indicators such as those of the BCLC.



## 1. Introduction

Worldwide, hepatocellular carcinoma (HCC) is the fifth and seventh most frequently diagnosed cancer, and the second and sixth most frequent cause of cancer death in men and women, respectively [1,2]. Hepatectomy is recommended as the firstline curative therapy for HCC patients with well-preserved liver function [3]. But even after resection, the 5-year patient survival rates varied from 25%–55%, with 5-year recurrence rates of 60%–100% [4]. Although the risk of recurrence is not uniform for these patients, identification of predictive factors that are linked to outcomes may allow modification of surveillance strategies for particular subgroups. Therefore, identifying prognostic factors is the key issue for many oncologists.

To date, the Barcelona-Clínic Liver Cancer (BCLC) classification is the most recognized system linking the prognosis and treatments of HCC [3]. However, one study compared the model for the end-stage liver disease score, and showed that BCLC was limited for the prognosis for HCC patients treated by hepatectomy [5]. The assessment of tumour size and enhancement of cross-sectional imaging has been the mainstay of oncological imaging evaluations in clinical practice [3]. However, these assessments were far from perfect

*Abbreviations:* HCC, hepatocellular carcinoma; BCLC, Barcelona-Clínic Liver Cancer; HAP, hepaticarterial phase; PVP, portal venous phase; ROC, receiver operating characteristic; AIC, akaike information criteria; OS, overall survival; DFS, disease free survival; TACE, trans-catheter arterial chemoembolization; PACS, picture archiving and communication system; ALT, alanine aminotransferase; AFP, alpha-fetoprotein; GLCM, gray level co-occurrence matrix; ROI, region of interest; HR, hazard ratio.

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because their prognostic value was limited by the lack of detailed quantitative parameters. Therefore, identifying reliable quantitative prognostic markers remains a difficult but important goal.

Previous studies have shown that computed tomography (CT) textural image features augmented the classification of pulmonary parenchyma as normal or abnormal [6], part-solid ground-glass nodules, pre-invasive, or invasive [7], and mediastinal lymph nodes as benign or malignant [8]. Baseline and initial post-treatment variations of CT texture parameters correlated with the response to therapy in parotid glands [9], advanced non-small cell lung cancer [10], and oesophageal cancer [11], and could be an independent predictive factor for survival in colorectal cancer [12–14], metastatic renal cell cancer [15], and locally advanced squamous cell carcinoma of the head and neck [16].

To the best of our knowledge, there were few studies regarding texture analyses for HCC prognoses. We hypothesized that intrinsic heterogeneity and edge variation for primary HCC tumours might yield predictive information. By measuring baseline texture parameters in the arterial phase (HAP), and portal venous phase (PVP), as well as changes between the two phases (HAP-PVP, Dif) at three different filters (0,1.0, and1.5), the CT texture features of primary HCC might be potential independent markers for survival. To confirm this hypothesis, we performed this retrospective study in patients with a single HCC treated by hepatectomy.

## 2. Materials and methods

### 2.1. Ethics approval

Ethical approval was obtained for this retrospective analysis, and the need to obtain informed consent was waived.

### 2.2. Patients

The study population consisted of patients diagnosed with HCC and treated at our hospital between September 2007 and January 2012. All the data were derived from the electronic medical records and radiology data (Fig. 1).

The inclusion criteria were: 1) diagnosed with HCC; 2) having a single lesion; 3) BCLC stage of up to B with hepatectomy as the initial treatment; 4)postoperative survival >3 months; 5) follow-up for at least 3 years if no recurrence; 6) having regular follow-ups until death; and 7) having preoperative hepatic CT images with 1.25 mm thickness. The exclusion criteria were: 1) an unrecorded baseline CT; 2) having multiple lesions; 3) previously treated by trans-catheter arterial chemoembolization (TACE) or ablation; 4) other accompanying cancer besides HCC; 5) included chest or lower abdominal examinations; and 6) lack of thin slice images of 1.25 mm.

### 2.3. CT examinations

All baseline images retrieved from the picture archive and communication system (PACS) database were analysed by conventional contrast enhanced hepatic CT using one scanner (LightSpeed VCT-64, GE Medical Systems, Waukesha, WI, USA).Post-contrast CT images were obtained after the administration of a non-ionic contrast agent (Iopamiro 370; 370 mg/mL; 1.5 mL/kg body weight)according to the patient's weight, and using no more than 100 mL with a pump injector at 3.5 mL/s. The upper abdomen was imaged in the arterial phase of enhancement (25 s delay), and the portal venous phase used a 70 s delay. The standard imaging protocol at our institution used the following scan parameters:120 kV; automatic mA adjustment; pitch, 0.984; 0.6 s rotation time; 5 mm collimation; field of view, 300 mm; matrix, 512. Reconstructed images of 1.25 mm were transferred to two personal computers for texture analyses.

All baseline CT examinations were performed within 14 days before surgery. When more than one compliant preoperative CT examination was available, we chose the latest one for further analysis.

### 2.4. Survival strategies

The primary endpoint was overall survival (OS); the secondary endpoint was disease free survival (DFS). All recurrences were confirmed by CT. The OS was defined as the time span from the baseline CT to the death or the end date. The DFS was defined as the time span from the baseline CT to recurrence or the end date. The TACE and ablation were scheduled if necessary after recurrence. Patients were followed up until death or March 2015 if they were still alive.

### 2.5. Radiographic and clinical variables

We carefully chose the following enhanced CT imaging features of HCC: shape (invasive or non-invasive), capsule (integrated or not), corona (positive or negative), mosaic (positive or negative), enhance region (<25%, 25%–50%, 50%–75%, and >75%)according to the literature [17,18], as well as clinical data[alanine aminotransferase (ALT), alpha-fetoprotein (AFP), neutrophils/lymphocytes ratio (N/L), Child–Pugh score, BCLC, cirrhosis, and hepatitis type].

### 2.6. Computerized texture analyses

The thin section CT images of 1.25 mm were loaded and analysed with MATLAB 2014a (Mathworks, Natick, MA, USA) before and after the application of Laplacian and Gaussian spatial band-pass filters. The process was comprised of two steps: 1) image filtration; and 2) quantification of texture. This resulted in derived CT texture images displaying imaging features at three scales in the regions of interest (ROIs). ROI was delineated around the tumour outline at the longest dimension as depicted on a series of derived images displaying texture features corresponding to different filters.

In this study, we investigated three algorithms [Gray level co-occurrence matrix (GLCM), Gabor, and Wavelet] to quantitatively evaluate the textural characteristics. The textural features of the Gabor (Scale1.1–3.4), the Wavelet (1–9), and the GLCM (kurtosis, skewness, contrast, correlation, entropy, energy, and homogeneity) algorithms are shown in the appendix. These features were selected based on previous studies. The data from the HAP and PVP (Dif) obtained by texture analyses at baseline CT were also derived.

### 2.7. Statistical analyses

SPSS, version 20.0 (IBM SPSS, Armonk, NY, USA) and R version 3.2.0 (R Foundation for Statistical Computing, Vienna, Austria) for windows were used for statistical analyses. Independent-sample *t*-tests (for quantitative data with normality, such as albumin at baseline), Mann–Whitney *U* tests (for ranked data or quantitative data without normality, such as age/BCLC, stage/Child–Pugh score/Total bilirubin at baseline, and during treatment), or chi-squared tests (for binomial distribution data, such as gender at baseline) were used as appropriate. The Cohen's kappa statistic was used to test the consistency between the two radiologists. The scale for κ value was as follows: κ value <0.20, poor agreement; κ value 0.21–0.40, fair agreement; κ 0.41–0.60, moderate agreement; κ 0.61–0.80, good agreement; and 0.81–1.00, excellent agreement.

The receiver operating characteristic (ROC) was used to screen the texture parameters dichotomized by 3-year survival and to obtain the optimal cut-off value (threshold). The parameters with