THE SIGNIFICANCE OF QUANTIFIED EXTRACELLULAR MATRIX FEATURES IN PATIENTS WITH HEPATOCELLULAR CARCINOMA AFTER CURATIVE LIVER RESECTION

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Background / Aim

Survival of patients with hepatocellular carcinoma (HCC) had been gradually improved because of a rapid growth in treatment options in recent years. In the era of precision medicine, there is a need of systematic approach for more personalized treatment based on efficacy and costs. Utilizing digital pathological system to examine dynamics of extracellular matrix (ECM), i.e. qFibrosis, has recently been validated in drug development for Nonalcoholic steatohepatitis. Therefore, we aim to demonstrate a histopathological evidence-based approach to fulfil this need.

Methods

Normal liver tissue and liver tumor from 203 patients with HCC who underwent curative tumor resection were imaged and assessed using qFibrosis system [1], which later generated a total of 33 and 156 collagen parameters from normal liver tissue and tumor part, respectively. We used these collagen parameters to build two models, (RFS-index and OS-index) for prediction of patient's recurrence-free survival (RFS) and overall survival (OS) years. The models were validated using leave-one-out method.

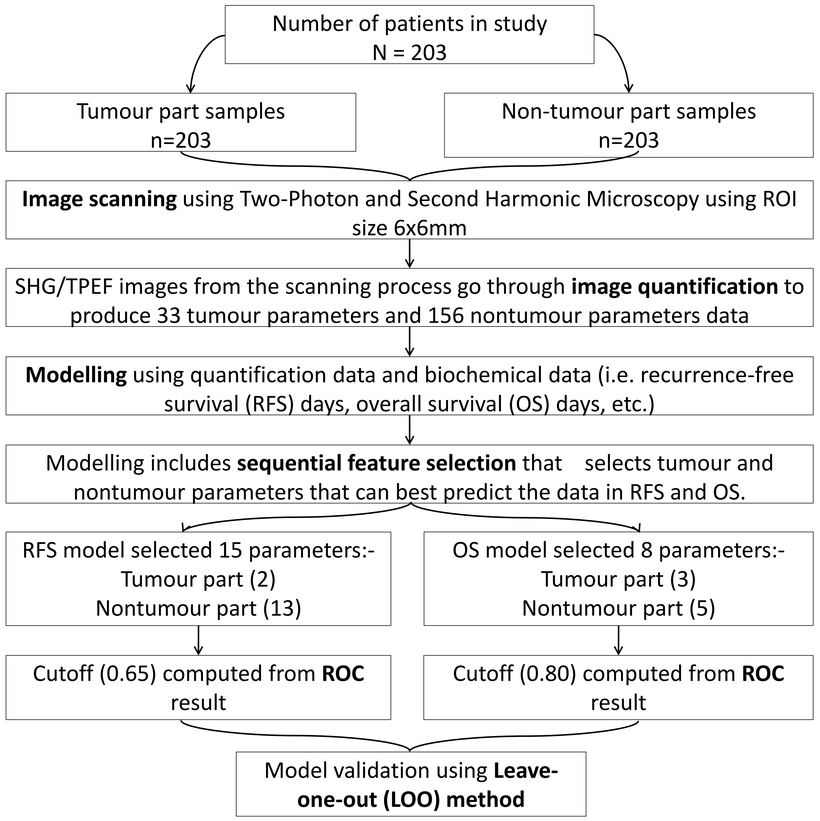

Figure 1. Flowchart of methods.

Model	ParameterName	Parameter Description
RFS Model	%Dis	Percentage of distributed collagen for overall fibrosis in tissue area
	#ShortStr	Number of short strings for overall fibrosis unit tissue area
	#Intersection	Number of short strings for peri-portal fibrosis per unit tissue area
	#ShortStrPT	Length of all strings for peri-portal fibrosis per unit tissue area
	#ThinStrPTAgg	Number of distributed strings for peri-portal fibrosis per unit tissue area
	#LongStrPTDis	Width of distributed for peri-portal fibrosis per unit tissue area
	#ThickStrPTDis	Percentage of total collagen for zone 2 fibrosis in tissue area
	%PeriPortalAgg	Number of thin strings for zone 2 fibrosis per unit tissue area
	#ThickStrPeriPortalDis	Percentage of total collagen for peri-central fibrosis in tissue area
	StrWidthPeriPortalDis	Number of strings for peri-central fibrosis per unit tissue area
	#ShortStrPeriCentral	Length of all strings for CV fibrosis per unit tissue area
	#ShortStrPeriCentralAgg	Length of aggregated for CV fibrosis per unit tissue area
	#ThickStrPeriCentralDis	Percentage of total collagen for chickenwire fibrosis in tissue area
	StrLengthCVAgg	Number of thin and distributed for chickenwire fibrosis per unit tissue area
	#LongStrCVDis	Width of distributed for chickenwire fibrosis per unit tissue area
OS Model	#ShortStr	Number of short strings for overall fibrosis unit tissue area
	#ThickStr	Number of thick strings for overall fibrosis unit tissue area
	ratio #ThickStr/#ThinStr	Area of aggregated for portal tract fibrosis per unit tissue area
	StrSolidity	Percentage of aggregated collagen for peri-portal fibrosis in tissue area
	#LongStrZone2Dis	Width of distributed for peri-central fibrosis per unit tissue area
	#ThinStrCV	Number of aggregated strings for chickenwire fibrosis per unit tissue area
	StrAreaCVAgg	Number of long and distributed for chickenwire fibrosis per unit tissue area
	#ThinStrCVDis	Number of intersections of all strings for chickenwire fibrosis per unit tissue area

Table 1. Selected parameters

Results

The RFS-index can differentiate the patients with RFS>2 years (n=131) and RFS≤2 years (p<0.001) with a cut-off value RFS-index=0.65.

The OS-index can also differentiate the patients with OS>3 years (n=152) and OS≤3 years (p=0.013) with a cut-off value OS-index=0.8.

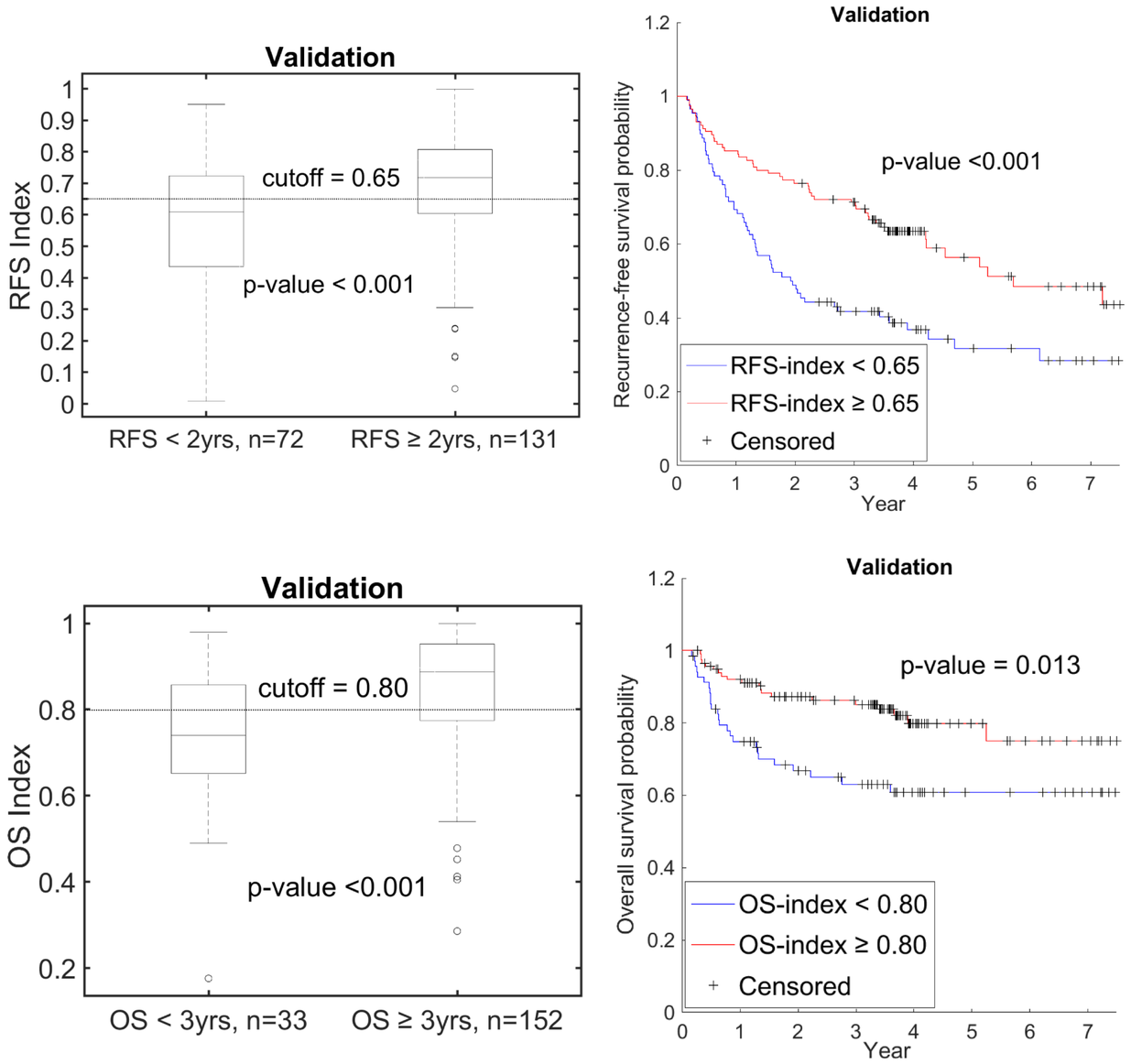

Figure 2. Validation set of RFS-index and OS-index models.

Discussion

In the era of precision medicine, personalized differences of each patient need to be addressed in cancer treatment. Many prognostic factors for HCC have been proposed and widely used in clinical practice, such as AFP, cancer stage, tumor grade and differentiation. However, there is still a lack of histopathological characteristics from the patient himself. qFibrosis of both tumor and non-tumor parts of the liver fulfills this unmet need. In combination with other clinical parameters, personal differences get further emphasized through analyzing fibrosis characteristics in HCC patients.

Conclusion

We demonstrate the capability of a histopathological evidence-based evaluation on HCC patient outcome. The quantified ECM features of HCC patients (along with other clinical and biochemical data such as tumour staging, alpha-fetoprotein, etc.) appear to be an important parameter which could help to build a system of a cost-effective and personalized treatment platform.

1. Liu F, Goh G, Tiniakos D, Wee A, Leow W, Zhao J, Rao H, et al. qFIBS: An Automated Technique for Quantitative Evaluation of Fibrosis, Inflammation, Ballooning, and Steatosis in Patients With Nonalcoholic Steatohepatitis. 2020;71:1953-1966.

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