CT Radiomics Improves Survival Prediction in Colorectal Liver Metastases: Beyond Clinical Scores

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Supplementary Material

Supplementary Text 1. Details of the evaluated scoring systems

- **FONG Score** (+1 point per item; low-risk 0-2 points, high-risk 3-5 points): node-positive primary, disease-free interval from primary to metastases <12 months, number of hepatic tumors >1, largest hepatic tumor >5 cm, carcinoembryonic antigen level >200 ng/ml.

- **GAME Score** (low-risk 0-1 points, intermediate-risk 2-3 points, high-risk 4+ points): KRAS-mutated tumors (1 point), carcinoembryonic antigen level ≥ 20 ng/ml (1 point), node-positive primary (1 point), Tumour Burden Score 3-8 (1 point) or ≥ 9 (2 points), extrahepatic disease (2 points).

- **RAS Mutation Clinical Risk Score** (+1 point per item): node-positive primary, RAS-mutated tumors, largest hepatic tumor >5 cm.

Supplementary Text 2. Image acquisition protocol

The analysed CT scans were acquired according to a standardized protocol: breath-holding acquisitions, including a pre-contrast basal phase, a bolus-triggered arterial phase, a portal phase (75 seconds after contrast administration) and a late phase (3 minutes after contrast administration). The iodine contrast media (Iomeron 300 mg/ml, Bracco Imaging, Italy) injected in bolus, followed by a 30-ml 0.9% saline solution flush. To time arterial phase acquisitions, bolus tracking over the abdominal aorta near the celiac trunk was used, with a threshold of 120 Hounsfield units. CT images were acquired on three different devices (Philips and GE Healthcare) with a similar set-up in terms of detector collimation (0.625 mm), current (280–400 mA), tension (120–140 kV) and pitch (0.975). We also used automatic exposure control based on the X-ray attenuation on scout images.

Supplementary Text 3. Radiomic feature extraction

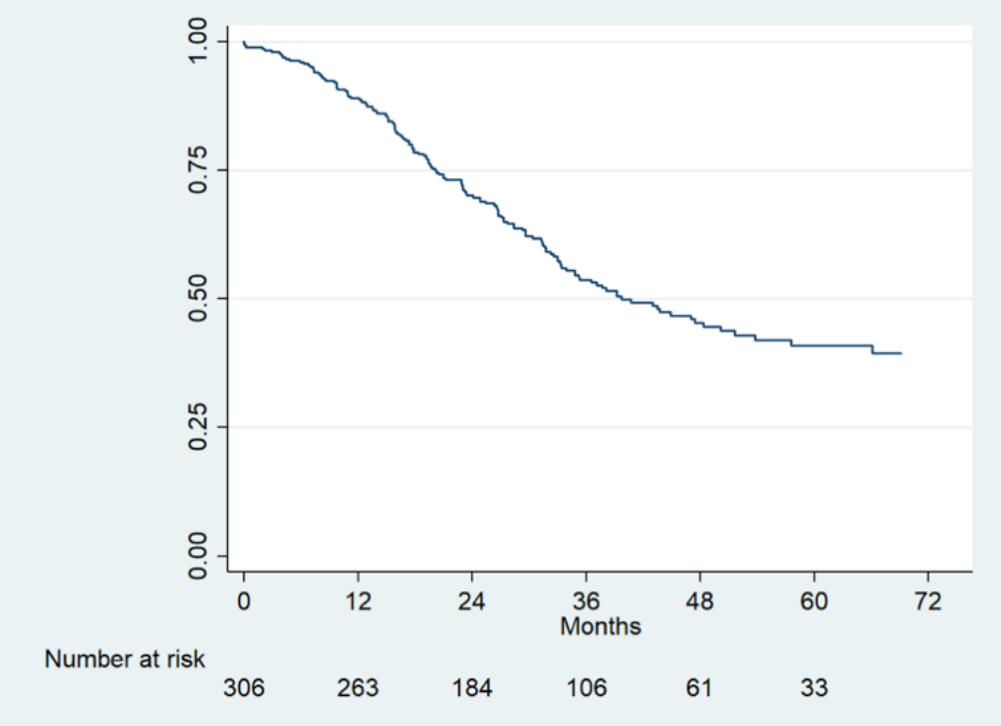
Radiomic features were extracted using the IBSI-compliant software LIFEx v7.5. Unless otherwise specified, all parameters were kept at the software default. Gray-level discretization was performed with a fixed bin width of 10 within an absolute intensity range of −1000 to 3000 HU, with textural features computed in 3D. No image resampling was applied. Features were derived exclusively from the original portal venous phase CT images (Tumor-VOI and 5-mm peritumoral Margin-VOI), without any additional filtering or transformed image types.

Supplementary Text 4. Analysed clinical variables

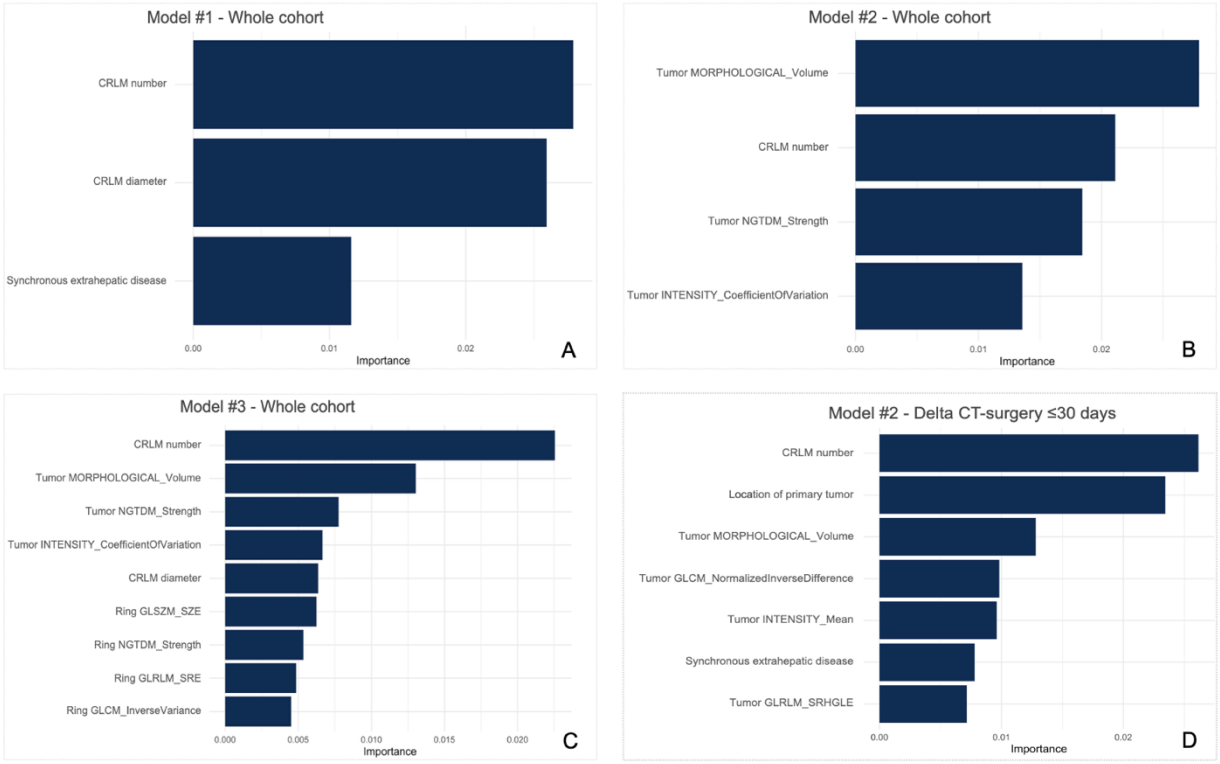
The analysed clinical variables included the following parameters:

- Demographic data - sex and age
- Primary tumor - sidedness, T status, and N status
- Liver metastases characteristics - synchronous/metachronous, number, and size at surgery
- Concomitant extra-hepatic disease
- Mutational status of KRAS, NRAS, and BRAF
- Pre-operative CEA value
- Pre-operative chemotherapy data - administration, regimen, number of lines and cycles, and radiological response (RECIST v1.1)
- CT-surgery interval
- Post-operative data – 90-day mortality, infective/severe morbidity, resection margins (R0/R1), adjuvant chemotherapy.

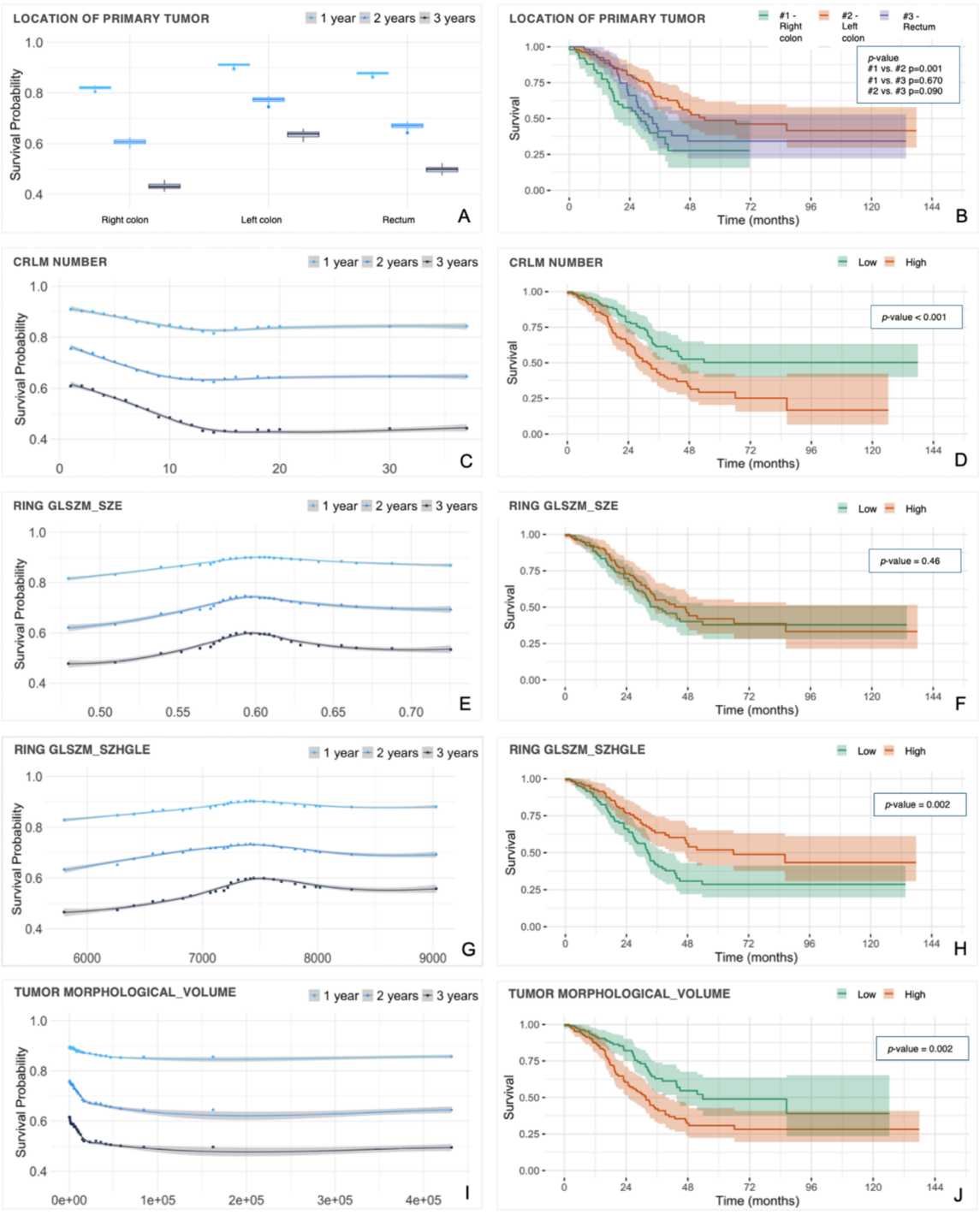
Supplementary Figure 1. Kaplan–Meier curve for overall survival



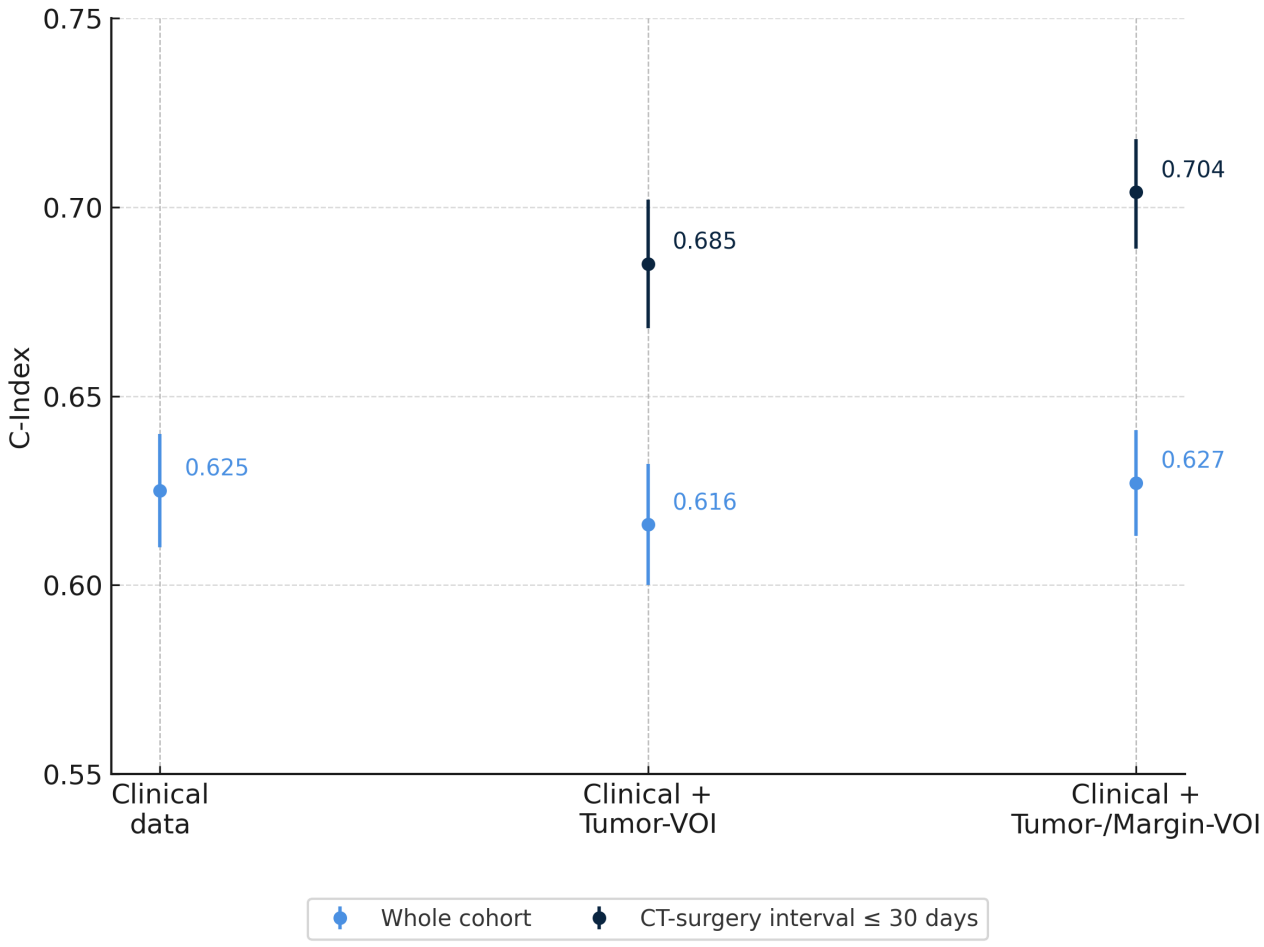
Supplementary Figure 2. Feature importance plots of the developed models in the whole cohort (A - pure clinical, B - combined clinical and Tumor-radiomics, C - combined clinical and Tumor/Margin-radiomics) and in the subgroup of patients with a CT-surgery interval ≤ 30 days (D - combined clinical and Tumor-radiomics)



Supplementary Figure 3. Partial Effect plot (A, C, E, G, I) and Kaplan-Meyer (B, D, F, H, J) of the five most important variables of Model #3 (combined clinical and Tumor/Margin-radiomics) in the subgroup of patients with the CT-surgery interval ≤ 30 days. The median split values for the Kaplan-Meyer curves were as follows: 3 lesions for CRLM number; 0.597 for Ring GLSZM_SZE; 7314.81 for Ring GLSZM_SZHGLE; 10678.23 mm3 for Tumor MORPHOLOGICAL_Volume



Supplementary Figure 4. Performance of the models (c-index and 95% CI) including a heterogeneity-based stratification variable (stdCoreCa3) in the whole cohort (light blue) and in the subgroup of 212 patients with a CT-surgery interval ≤ 30 days (blue)



Supplementary Table 1. CLEAR Checklist

Section	No.	Item	Yes	No	n/a	Page
Title						
	1	Relevant title, specifying the radiomic methodology	X	☐	☐	1
Abstract						
	2	Structured summary with relevant information	X	☐	☐	2-3
Keywords						
	3	Relevant keywords for radiomics	X	☐	☐	3
Introduction						
	4	Scientific or clinical background	X	☐	☐	4
	5	Rationale for using a radiomic approach	X	☐	☐	4
	6	Study objective(s)	X	☐	☐	4
Method						
Study Design	7	Adherence to guidelines or checklists (e.g., CLEAR checklist)	X	☐	☐	5
	8	Ethical details (e.g., approval, consent, data protection)	X	☐	☐	5
	9	Sample size calculation	X	☐	☐	6
	10	Study nature (e.g., retrospective, prospective)	X	☐	☐	5
	11	Eligibility criteria	X	☐	☐	5
	12	Flowchart for technical pipeline	X	☐	☐	Fig 1
Data	13	Data source (e.g., private, public)	X	☐	☐	5
	14	Data overlap	☐	X	☐	-
	15	Data split methodology	☐	☐	X	-
	16	Imaging protocol (i.e., image acquisition and processing)	X	☐	☐	S.Text 2
	17	Definition of non-radiomic predictor variables	X	☐	☐	S.Text 4
	18	Definition of the reference standard (i.e., outcome variable)	X	☐	☐	5, 7
Segmentation	19	Segmentation strategy	X	☐	☐	6
	20	Details of operators performing segmentation	X	☐	☐	6
Pre-processing	21	Image pre-processing details	☐	X	☐	-
	22	Resampling method and its parameters	☐	X	☐	-
	23	Discretization method and its parameters	X	☐	☐	S.Text 3
	24	Image types (e.g., original, filtered, transformed)	X	☐	☐	S.Text 3
Feature extraction	25	Feature extraction method	X	☐	☐	7, S.Text 3
	26	Feature classes	X	☐	☐	7
	27	Number of features	X	☐	☐	7
	28	Default configuration statement for remaining parameters	X	☐	☐	S.Text 3
Data preparation	29	Handling of missing data	X	☐	☐	7
	30	Details of class imbalance	☐	☐	X	-
	31	Details of segmentation reliability analysis	X	☐	☐	6
	32	Feature scaling details (e.g., normalization, standardization)	☐	X	☐	-
	33	Dimension reduction details	X	☐	☐	8
Modeling	34	Algorithm details	X	☐	☐	8

	35	Training and tuning details	☐	X	☐	-
	36	Handling of confounders	☐	X	☐	-
	37	Model selection strategy	X	☐	☐	8
Evaluation	38	Testing technique (e.g., internal, external)	X	☐	☐	8
	39	Performance metrics and rationale for choosing	X	☐	☐	8
	40	Uncertainty evaluation and measures (e.g., confidence intervals)	X	☐	☐	8
	41	Statistical performance comparison (e.g., DeLong's test)	☐	X	☐	-
	42	Comparison with non-radiomic and combined methods	X	☐	☐	8
	43	Interpretability and explainability methods	X	☐	☐	8
Results						
	44	Baseline demographic and clinical characteristics	X	☐	☐	10, Table 1
	45	Flowchart for eligibility criteria	X	☐	☐	Fig 2
	46	Feature statistics (e.g., reproducibility, feature selection)	X	☐	☐	Fig. 5, S.Fig. 2
	47	Model performance evaluation	X	☐	☐	10-11, Table 2, Fig. 3, S.Fig. 3
	48	Comparison with non-radiomic and combined approaches	X	☐	☐	10-11, Table 2, Fig. 3, S.Fig. 3
Discussion						
	49	Overview of important findings	X	☐	☐	13
	50	Previous works with differences from the current study	X	☐	☐	13-15
	51	Practical implications	X	☐	☐	15-16
	52	Strengths and limitations (e.g., bias and generalizability issues)	X	☐	☐	15-16
Open Science						
Data availability	53	Sharing images along with segmentation data [n/e]	☐	X	☐	-
	54	Sharing radiomic feature data	☐	X	☐	-
Code availability	55	Sharing pre-processing scripts or settings	☐	X	☐	-
	56	Sharing source code for modeling	☐	X	☐	-
Model availability	57	Sharing final model files	☐	X	☐	-
	58	Sharing a ready-to-use system [n/e]	☐	X	☐	-