Supplementary Materials

Scoping review of digital pathology for neoadjuvant rectal cancer response

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This supplementary file reports the complete database search strategy, funding information reported by the included studies, and model operating characteristics.

Supplementary Table 1. Complete database search strategy

Database	Interface	Search date	Limits
PubMed	National Library of Medicine	17 February 2026	English; 17 February 2016 to 17 February 2026
Embase	Elsevier	17 February 2026	English; 17 February 2016 to 17 February 2026
Cochrane Library	Wiley	17 February 2026	English; 17 February 2016 to 17 February 2026
Exact free-text Boolean search string used in all three databases: ((rectal cancer) OR (colorectal cancer) OR (rectal adenocarcinoma)) AND ((neoadjuvant) OR (chemoradiotherapy) OR (treatment response) OR (pathological complete response) OR (tumor regression grade)) AND ((histology) OR (pathology) OR (whole slide imaging) OR (WSI) OR (biopsy)) AND ((artificial intelligence) OR (deep learning) OR (machine learning) OR (computer vision))			

The same free-text Boolean search string was entered into each database interface. The English-language and publication-date limits shown above were applied.

Supplementary Table 2. Reported thresholds and operating characteristics

Publication and model	Cohort and target	Cutoff	Sensitivity	Specificity	PPV	NPV	Calibration/DCA
Feng[13] Nuclear pathomics	Prospective *n* = 100; pCR	NR	0.868 (0.721-0.999)	0.715 (0.613-0.818)	0.468 (0.308-0.629)	0.918 (0.853-0.984)	NR/NR
Feng[13] Microenvironment	Prospective *n* = 100; pCR	NR	0.740 (0.397-0.999)	0.559 (0.163-0.956)	0.342 (0.180-0.505)	0.846 (0.745-0.948)	NR/NR
Feng[13] RAPIDS multimodal	Prospective *n* = 100; pCR	NR	0.888 (0.728-0.999)	0.740 (0.593-0.886)	0.512 (0.313-0.710)	0.929 (0.862-0.995)	NR/NR
Foersch[14] Multistain model	Cross-validation *n* = 117; response Dworak 3-4	NR	NR	NR	0.679[a]	0.781[a]	NR/NR
Jepsen[15]	Association analysis; complete/good response	NA	NA	NA	NA	NA	NA/NA
Lafarge[16]	imCMS association with pCR	NA	NR	NR	NR	NR	NA/NR
Lou[17] DeepPCR	External *n* = 102; pCR	> 0.7	0.725 (0.637-0.814)	0.627 (0.463-0.773)	0.758 (0.671-0.847)	0.536 (0.368-0.688)	NR/NR

Publication and model	Cohort and target	Cutoff	Sensitivity	Specificity	PPV	NPV	Calibration/DCA
Shao[18] Pathomics PS[b]	Pooled external *n* = 678; TRG 0 *vs.* TRG 1-3	NR	NR	NR	NR	NR	NR/NR
Wang[19] GNN/CNN	Internal validation *n* = 14; good *vs.* poor response; 500 tiles	NR	0.400	0.778	NR	NR	NR/NR
Wu[20] 40× model	TRG 0 class; split for these operating metrics unclear[c]	NR	0.67	0.95	0.67[c]	NR	NR/NR
Zhang 2020[21] Pathology signature	Internal validation *n* = 31; poor response	NR	0.700 (0.476-0.889)	0.727 (0.444-1.000)	NR	NR	Calibration curve reported/DCA reported
Zhang 2022[22] Multiscale MIL	Internal split; good *vs.* non-good response	NR	NR	NR	NR	NR	NR/NR
Zhang 2024[23] XGBoost	External *n* = 50; pCR	NR	NR	NR	NR	NR	NR for pCR[d]/NR

Values are proportions, with 95% confidence intervals in parentheses where reported. Values are reproduced from the original publications; missing estimates were not calculated. Cutoffs refer to predicted response probability. NR, not reported in the inspected material; NA, not applicable to the reported association analysis.

[a]Foersch's predictive values for response and non-response are shown as PPV and NPV, respectively, with response treated as positive.

[b]Shao *et al.*[18] reported sensitivity, specificity, PPV, and NPV (with 95%CIs, cutoff NR) for their multimodal RPS, but did not report these operating characteristics for the standalone PS.

[c]Wu reported precision, shown here as PPV. The evaluation dataset for these class-specific metrics was not clearly identified.

[d]Zhang *et al.* (2024)[23] reported calibration curves for a separate disease-free survival nomogram, but not for the pCR treatment-response classifier.

CI: Confidence interval; CNN: convolutional neural network; DCA: decision curve analysis; GNN: graph neural network; imCMS: image-based consensus molecular subtype; MIL: multiple instance learning; NPV: negative predictive value; pCR: pathological complete response; PPV: positive predictive value; PS: pathomics signature; RPS: radiopathomics signature; RAPIDS: radiopathomics integrated prediction system; TRG: tumour regression grade.

Supplementary Table 3. Funding information for included studies

Included study	Funding reported in the original article
Feng *et al.* (2022)[13]	National Natural Science Foundation of China (81872188, 81902867, 82001986, 81903152, 81922040, and 92059103); Youth Innovation Promotion Association of the Chinese Academy of Sciences (2019136)
Foersch *et al.* (2023)[14]	S.F. was supported by the Federal Ministry of Education and Research (16SV8167), the Stage-I-Program of the University Medical Center Mainz, the Mainz Research School of Translational Biomedicine, and the Manfred-Stolte-Foundation. J.N.K. was supported by the German Federal Ministry of Health (DEEP LIVER; ZMVI1-2520DAT111) and the Max-Eder Program of German Cancer Aid (70113864)

Included study	Funding reported in the original article
Jepsen *et al.* (2024)[15]	Carl and Ellen Hertz' Scholarship for Danish Medical and Natural Sciences; Lizzi and Mogens Staal Foundation; Else and Mogens Wedell-Wedellsborgs' Foundation; Folketingsmand Jens Christensen and wife Korna Christensens' Foundation; Inge and Jorgen Larsens' Memorial Scholarship; Manufacturer Einar Willumsen's Memorial Scholarship; Aase and Ejnar Danielsens' Foundation; Director Emil C. Hertz and wife Inger Hertz' Foundation; Harboe Foundation; Buschard Foundation; Kobmand Kristjan Kjaer and wife Margrethe Kjaers' Foundation; A. V. Lykfeldts and wifes' Scholarship; and Region Zealand Health Research Foundation
LaFarge *et al.* (2024)[16]	S:CORT consortium, jointly funded by the Medical Research Council and Cancer Research UK (MR/M016587/1); ARISTOTLE trial, funded by Cancer Research UK (CRUK/08/032); National Institute for Health Research Oxford Biomedical Research Centre; Research Fund of the Paracelsus Medical University Salzburg (PMU-FFFR-17/03/090-HUW); Health Data Research UK; EPSRC Centre for Doctoral Training in Health Data Science (EP/S02428X/1); Oxford CRUK Cancer Centre; Ludwig Institute for Cancer Research; Medical Research Council; Cancer Research UK; Swiss National Science Foundation (P2SKP3_168322/1 and P2SKP3_168322/2); and Promedica Foundation (F-87701-41-01)
Lou *et al.* (2022)[17]	Guangdong Science and Technology Project (2019B030316003); Natural Science Foundation of Guangdong Province (2019A1515010901); National Science Fund for Excellent Young Scholars (82122057); and Guangdong Natural Science Funds for Distinguished Young Scholars (2021B1515020022)
Shao *et al.* (2020)[18]	National Natural Science Foundation of China (81922040, 81930053, 81527805, and 81772012); Beijing Natural Science Foundation (7182109); National Key R&D Program of China (2017YFA0205200, 2017YFA0700401, and 2016YFA0100902); Strategic Priority Research Program of the Chinese Academy of Sciences (XDB32030200 and XDB01030200); Chinese Academy of Sciences (QYZDJ-SSW-JSC005 and KFJ-STS-ZDTP-059); and Youth Innovation Promotion Association of the Chinese Academy of Sciences (2019136)

Included study	Funding reported in the original article
Wang *et al.* (2023)[19]	National Key R&D Program of China (2019YFA0110601); National Natural Science Foundation of China (61977046); and Shanghai Municipal Science and Technology Major Project (2021SHZDZX0102)
Wu *et al.* (2023)[20]	National Natural Science Foundation of China (61906022); Chongqing Natural Science Foundation (cstc2020jcyj-msxmX0482); Chongqing University Research Fund (2021CDJXKJC004); and Chongqing Medical Scientific Research Project (2020MSXM088)
Zhang *et al.* (2020)[21]	National Key Research and Development Program of China (2017YFC1309100); National Science Fund for Distinguished Young Scholars (81925023); National Natural Science Foundation of China (81771912, 81671854, and 81702322); National Science Foundation for Young Scientists of China (81701782); and Key Research and Development Program of Guangdong Province (2018B030339001)
Zhang *et al.* (2022)[22]	Chinese Natural Science Foundation (61876166 and 61663046); Yunnan Provincial Major Science and Technology Special Plan Project (202002AD080001); Yunnan Basic Research Program for Distinguished Young Youths (202101AV070003); Yunnan Provincial Major Science and Technology Special Plan Projects: Digitization Research and Application Demonstration of Yunnan Characteristic Industry (202002AD080001); and Open Foundation of Key Laboratory in Software Engineering of Yunnan Province (2020SE304)
Zhang *et al.* (2024)[23]	Startup Fund for Scientific Research, Fujian Medical University (2021QH1077); Young and Middle-aged Backbone Training Project in the Health System of Fujian Province (2023GGA029); Special Financial Funds of Fujian Province (BPB-2023LX); and Talent Programs of the First Affiliated Hospital of Fujian Medical University (2022-YJRC3823)

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