

Interpretable Dynamic Host-Tumour Dual-Perspective Deep Learning for Predicting Pathological Response in NSCLC

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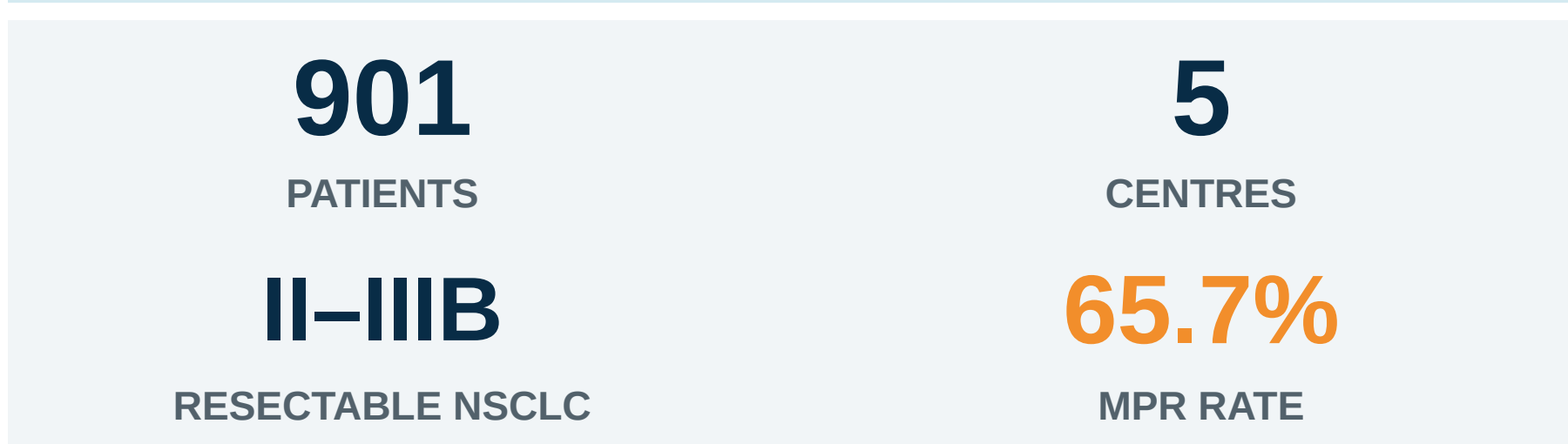
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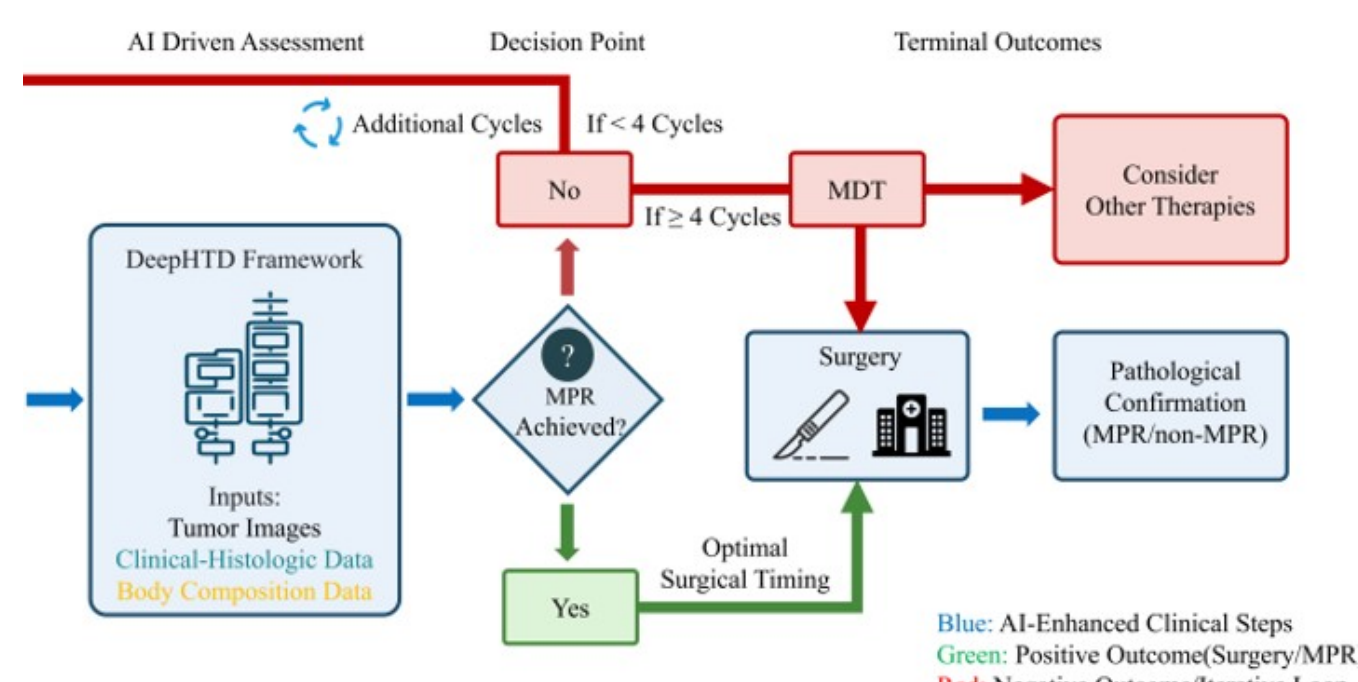
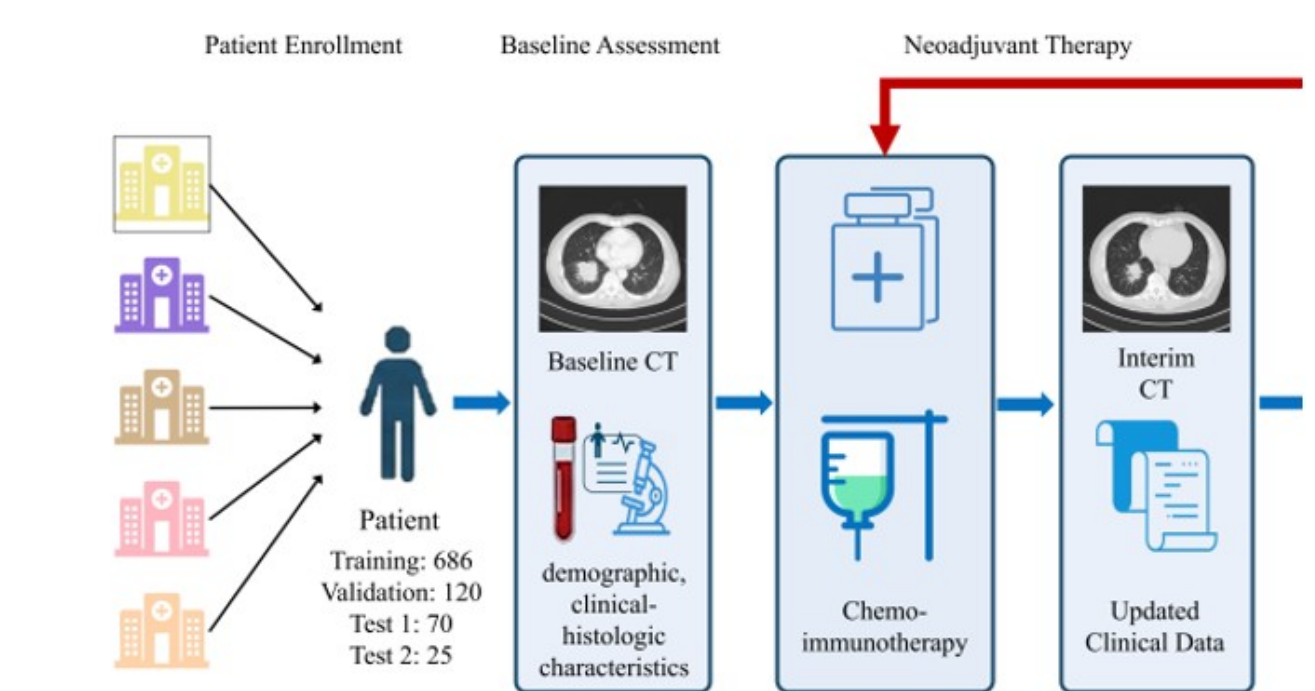
CLINICAL NEED

RECIST 1.1 measures size change—not residual viable tumour. Immune-related inflammation can obscure pathological regression. Most prediction models remain tumour-centric and overlook systemic host response.

STUDY DESIGN



Training 686 | Validation 120 | External tests 70 + 25



CLINICAL WORKFLOW | Interim assessment after neoadjuvant chemoimmunotherapy

Population Stage II–IIIB NSCLC from five centres

Treatment PD-(L)1 inhibitor + platinum chemotherapy

Imaging Paired baseline and interim HRCT, predominantly after 2–3 cycles

Reference Blinded postoperative pathological assessment

Endpoints Primary: MPR; secondary: EFS

INTERIM DECISION POINT | AFTER 2–3 CYCLES

STUDY QUESTION

Can paired interim CT reveal both tumour evolution and host immunometabolic change early enough to predict MPR before surgery?

WHY TWO VIEWS?

Dynamic tumour signal captures treatment-related remodelling.

Dynamic host signal quantifies SM, SAT, VAT and IMAT change across T1–L2.

Late fusion tests complementary evidence without hiding either branch.

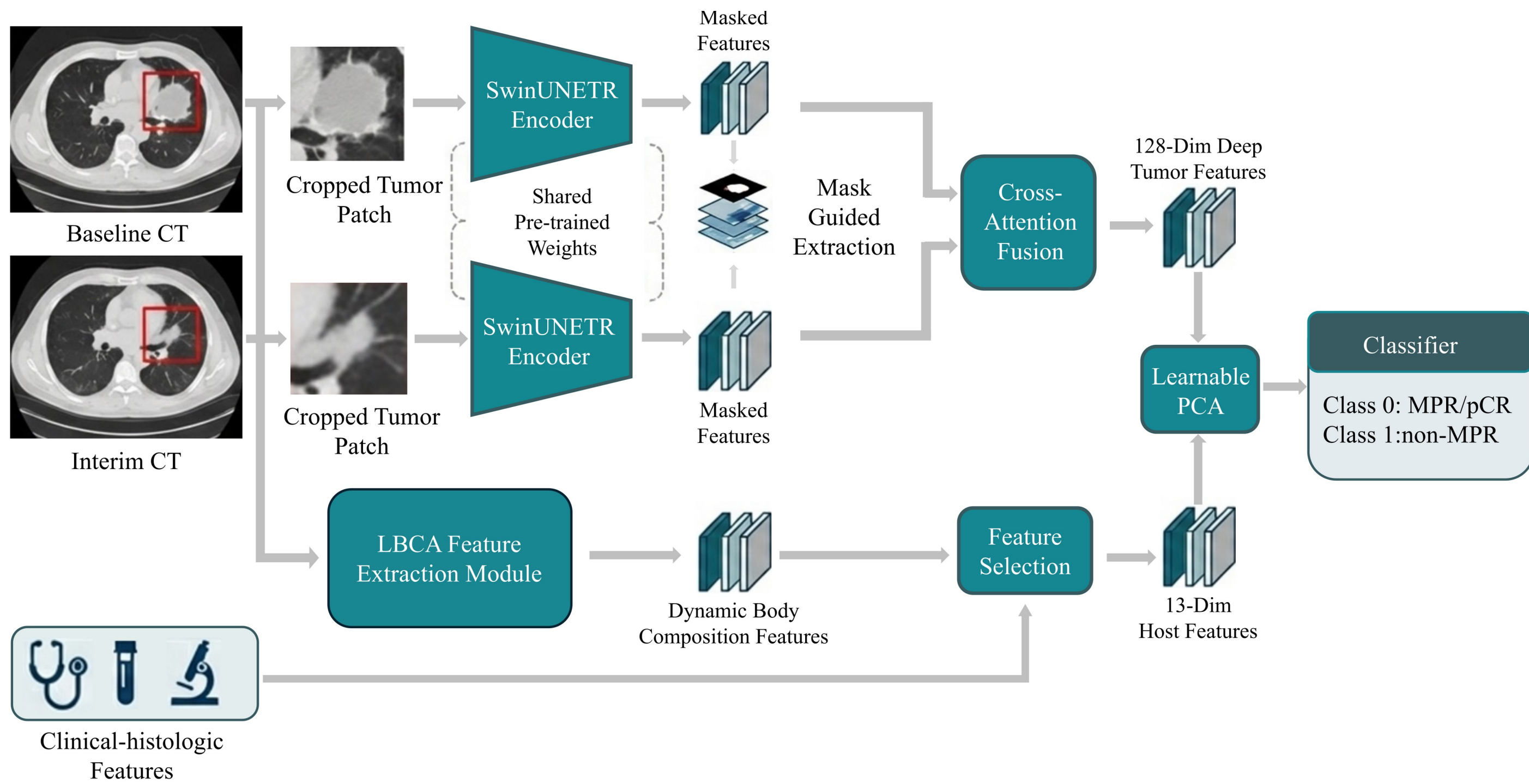
Clinical output is an individualized MPR / non-MPR probability before surgery.

DeepHTD | DYNAMIC HOST–TUMOUR DUAL PERSPECTIVE

Two separately interpretable longitudinal branches converge only after each has captured a distinct biological view of response.

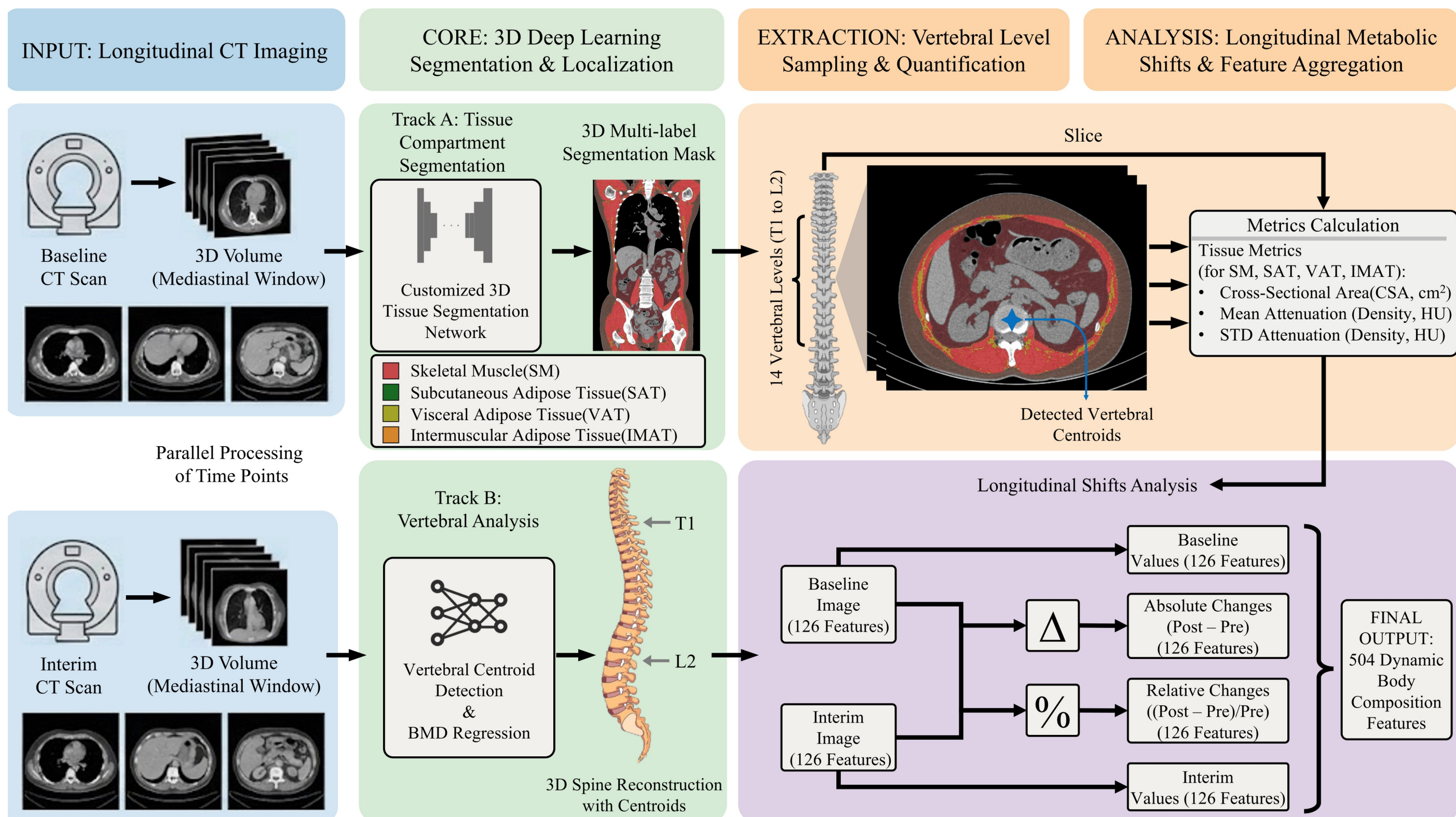
TUMOUR-EVOLUTION BRANCH · TE

Baseline + interim lung-window CT → shared SwinL-NETR encoders, mask guidance and cross-attention → 128-D evolution vector



HOST IMMUNOMETABOLIC BRANCH · IM

Paired mediastinal-window CT from T1 to L2 → SM, SAT, VAT and IMAT dynamics + clinical–histological variables → 13 host predictors

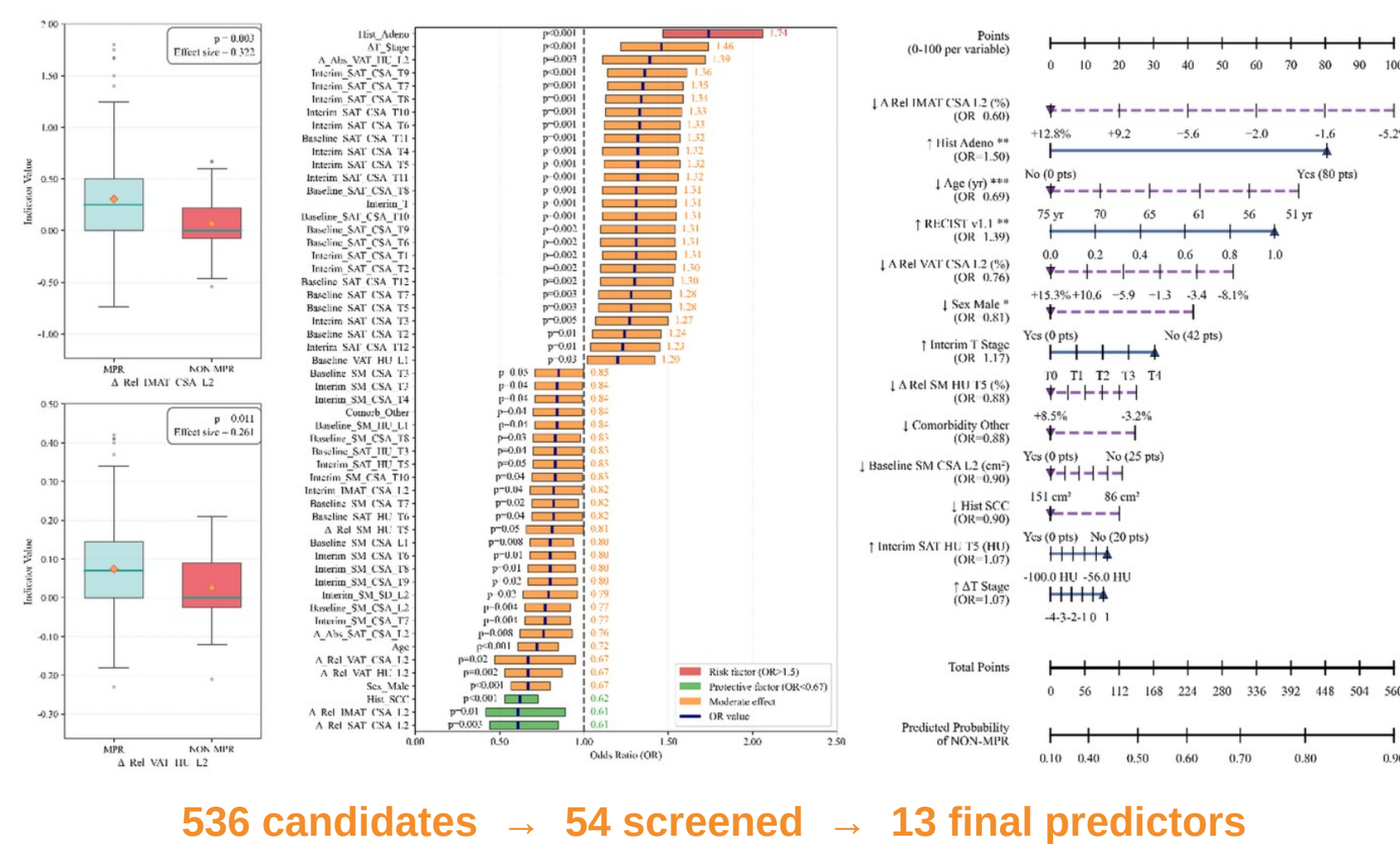


L-PCA + MULTIMODAL MLP FUSION → INDIVIDUALIZED MPR / NON-MPR PROBABILITY

Clinical interpretability is retained before fusion: each prediction can be interrogated at the tumour, feature and module levels.

PERFORMANCE & INTERPRETABILITY

1 | HOST FEATURE SELECTION



Highest-weight host predictor Δ Rel IMAT CSA at L2

The staged pipeline reduces high-dimensional host information before multimodal fusion.

3 | WHY THE PREDICTION IS TRUSTWORTHY

Tumour level Grad-CAM localizes treatment-related remodelling regions.

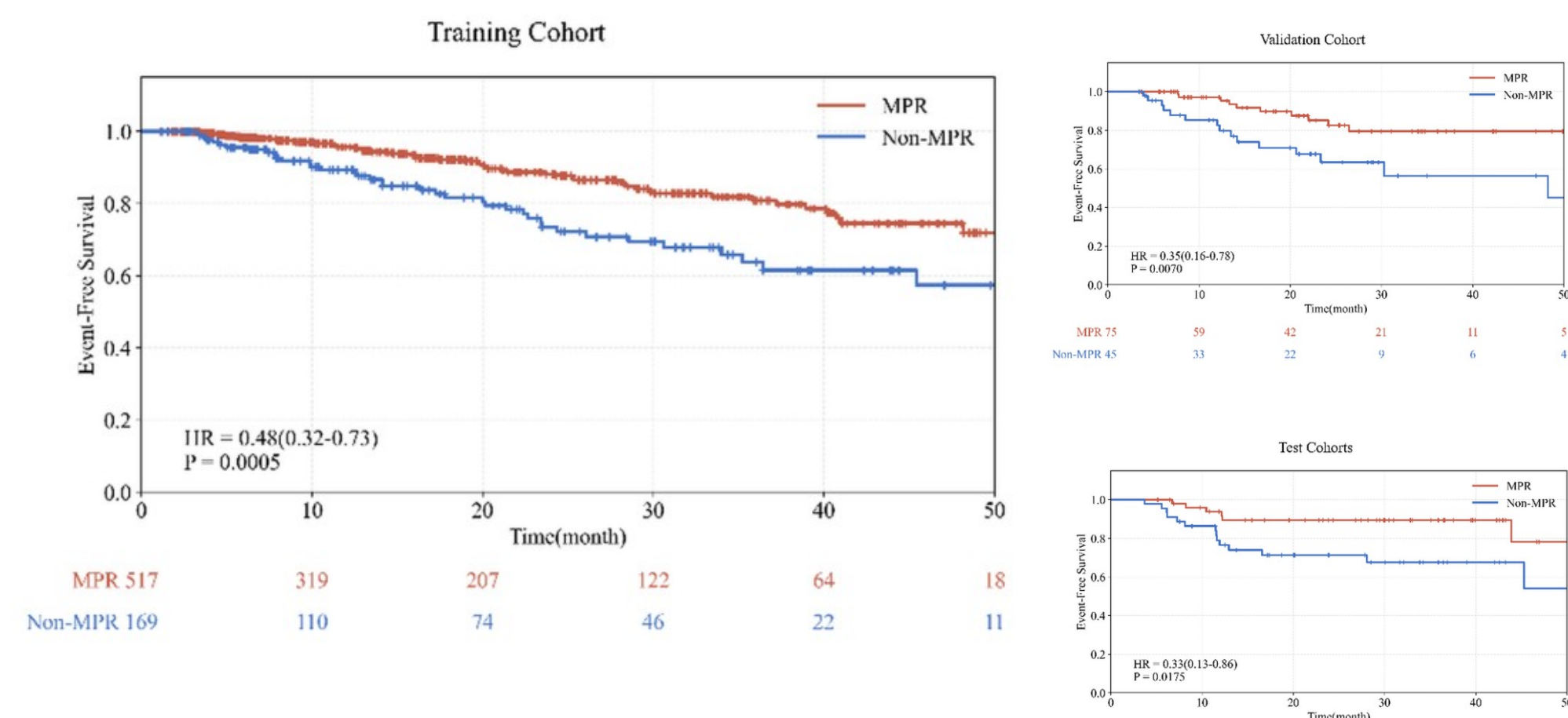
Feature level The L2 IMAT change is clinically identifiable and directionally interpretable.

Module level Host ablation: DeepTD AUC 0.752–0.797; tumour ablation: DeepHD AUC 0.690–0.774.

Selected → predicted → explained.

CLINICAL RELEVANCE

EFS STRATIFICATION BY PREDICTED RESPONSE



24-MONTH EFS · PREDICTED MPR vs NON-MPR

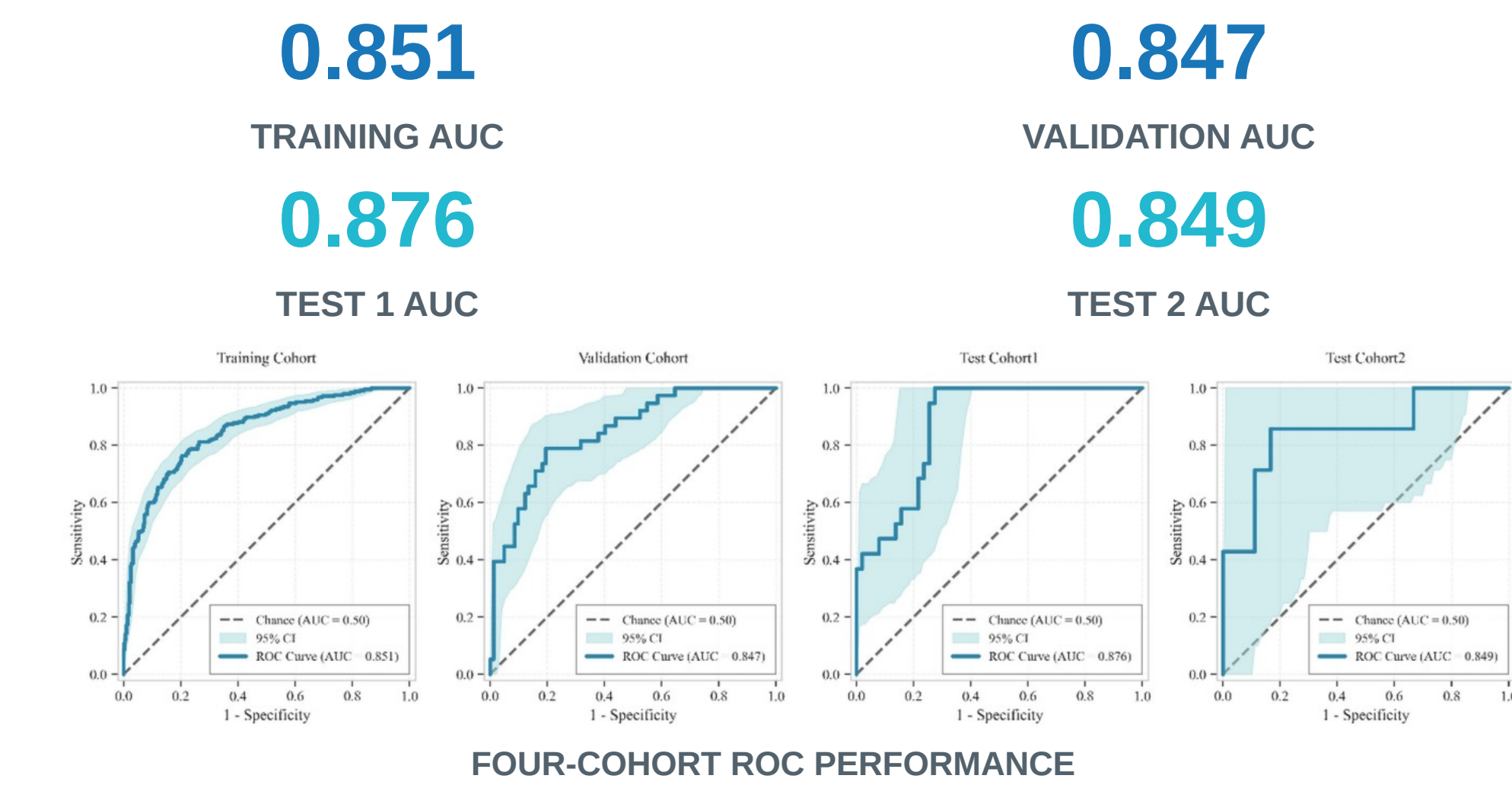
Training 88.1% vs 73.4% | Validation 85.1% vs 63.4%

Pooled tests 89.3% vs 71.3%

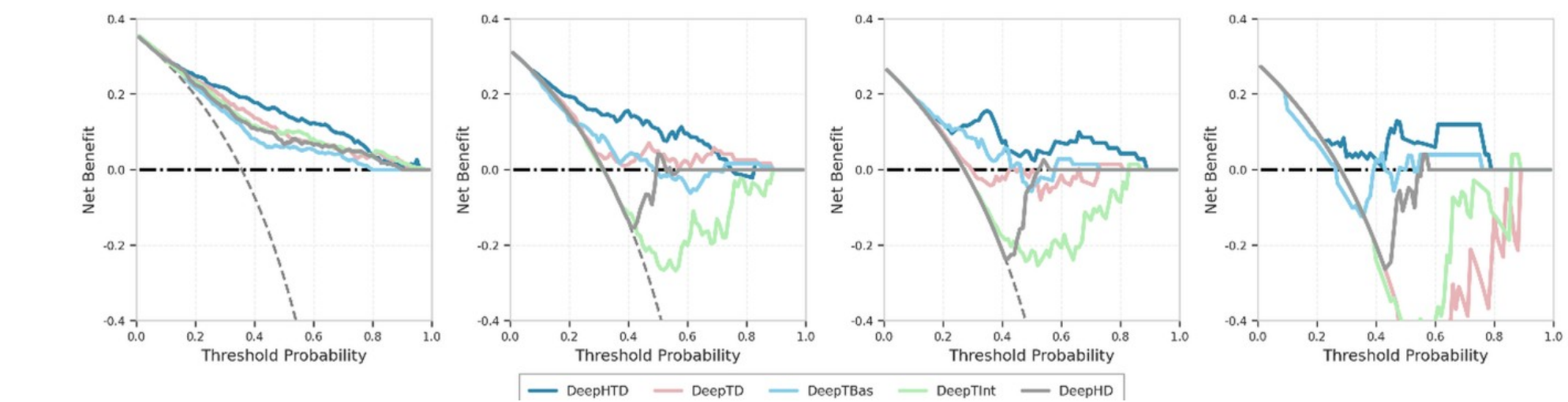
Adjusted HR 0.466 / 0.372 / 0.268

2 | PREDICTION PERFORMANCE

Stable discrimination from development through two independent external tests.

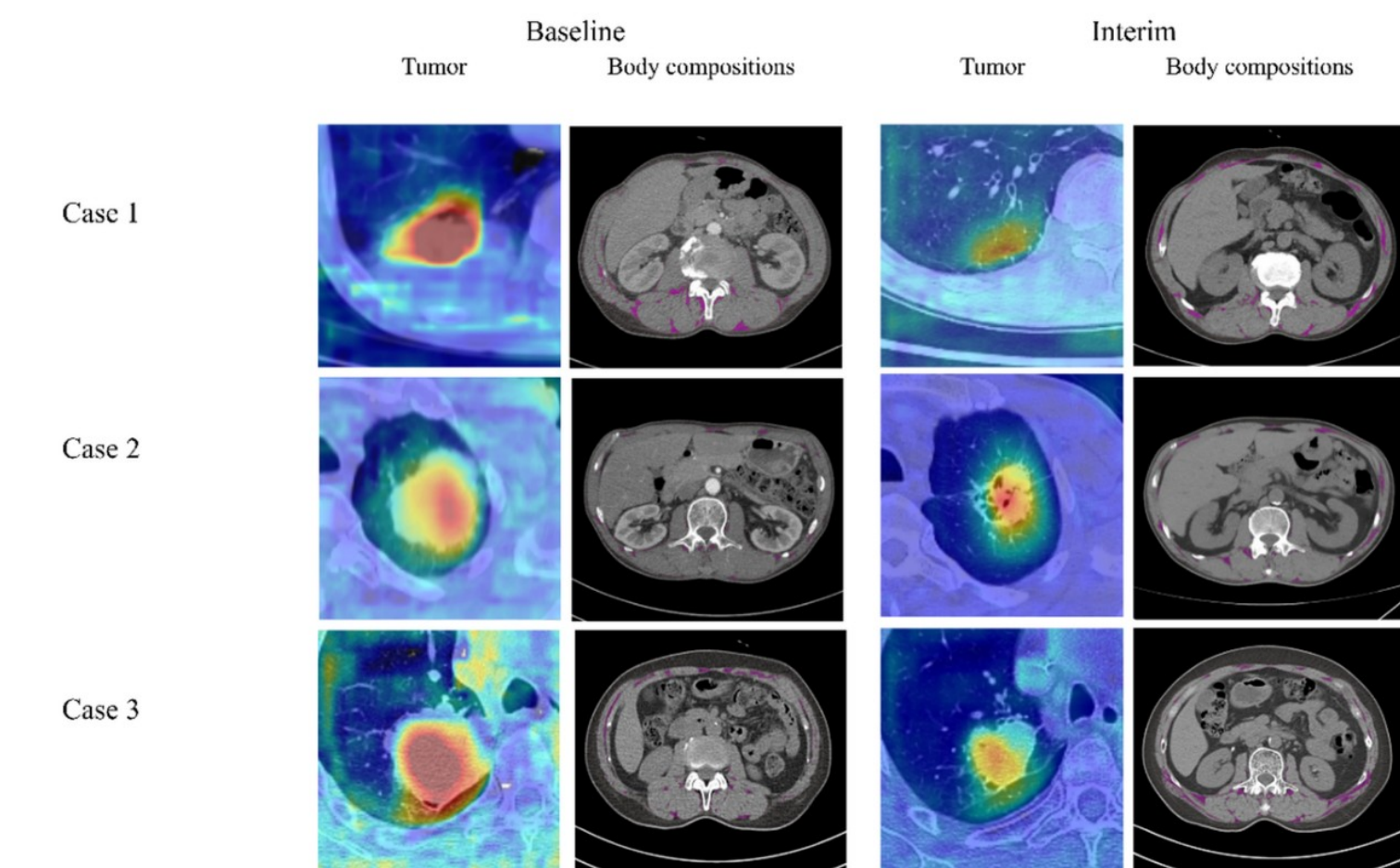


CLINICAL UTILITY | DECISION-CURVE ANALYSIS



DeepHTD provided greater net benefit than clinical staging and single-modality models across clinically relevant thresholds.

WHEN RECIST MISCLASSIFIES RESPONSE



Case 1: RECIST PR → pathology pCR. Cases 2–3: RECIST SD → pathology MPR. DeepHTD correctly reclassified all three using tumour heatmaps and host changes.

CLINICAL IMPLICATIONS

Adds an interim, pathology-oriented signal beyond tumour shrinkage.

May support risk-adapted timing of surgery or treatment modification after 2–3 cycles.

Designed as an interpretable adjunct to RECIST—not a replacement for multidisciplinary judgement.

TAKE-HOME

DeepHTD integrates dynamic tumour evolution with systemic host immunometabolic response, providing accurate and interpretable interim prediction of pathological response beyond RECIST.

Limitations: retrospective; Chinese and male-predominant; small Test 2 (n=25); prospective international, multiethnic validation and workflow calibration are required.

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