

AI-Driven Oncology Treatment Planning

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ABSTRACT

Oncology treatment planning integrates tumour biology, patient physiology, organ-at-risk tolerances, and rapidly evolving therapeutic options into decisions that determine survival and quality of life for cancer patients. The complexity of this integration has grown substantially with the advent of precision oncology, immunotherapy, and multimodal treatment combinations that create a decision space too large for unaided clinical judgement to navigate optimally. AI-driven treatment planning tools offer systematic optimisation across this decision space, from automated radiotherapy contouring and dose optimisation through ML-based systemic therapy sequencing and immunotherapy response prediction. We evaluated five AI treatment planning frameworks applied to 54,286 oncology patients at 18 European cancer centres in Berlin, Vienna, Paris, Stockholm, and Milan between 2017 and 2024, covering non-small cell lung cancer, breast cancer, rectal cancer, and head and neck cancer. Frameworks ranged from AI-assisted contouring in radiotherapy through fully integrated multimodal AI treatment planning with adaptive response-guided modification. Performance was benchmarked using our Oncology Treatment Planning AI Score (OTPAS), integrating plan quality, treatment delivery precision, tumour response rate, toxicity reduction, and clinical outcome improvement. The adaptive AI-integrated framework achieved the highest OTPAS (0.931), improving locoregional control at 2 years from 68.4% (standard planning) to 84.2% and reducing grade 3+ toxicity from 22.4% to 14.6%. Adaptive radiotherapy guided by mid-treatment MRI response showed the strongest tumour control advantage, while AI systemic therapy sequencing produced the largest quality-of-life benefit through toxicity-optimised regimen selection.

Keywords: AI treatment planning; oncology; radiotherapy; adaptive radiotherapy; systemic therapy; immunotherapy; NSCLC; breast cancer; rectal cancer; head and neck cancer; OTPAS; tumour control; toxicity reduction

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1. Introduction

1.1 The Treatment Planning Complexity Problem

Modern oncology treatment planning has become one of the most data-intensive clinical decision processes in medicine. A multidisciplinary tumour board for a locally advanced rectal cancer patient must integrate MRI staging, molecular profiling, mismatch repair status, carcinoembryonic antigen kinetics, pelvic anatomy for organ-at-risk dose constraints, patient performance status, comorbidities, and treatment intent to select between neoadjuvant chemoradiotherapy, total neoadjuvant therapy, short-course radiation followed by systemic therapy, or primary systemic therapy -- with different subsequent surgery or watch-and-wait implications for each path. The growth of precision systemic therapy options has multiplied this complexity further: for HER2-positive breast cancer, the choice between neoadjuvant versus adjuvant anti-HER2 therapy, CDK4/6 inhibitor combination, and escalation or de-escalation based on pathological complete response involves pharmacokinetic, toxicity, and survival considerations that evidence summaries alone cannot integrate for individual patients. AI treatment planning tools address this by systematically exploring the treatment decision space, optimising against multiple objectives simultaneously, and incorporating patient-specific factors that guideline recommendations average over. This study benchmarks five AI treatment planning frameworks across four tumour types and 54,286 patients to identify which approaches most reliably improve tumour control and reduce treatment toxicity.

1.2 Study Objectives

The aims were to benchmark five AI oncology treatment planning frameworks against OTPAS across 18 European cancer centres and four tumour types; to quantify locoregional control, toxicity, and survival improvements from adaptive AI-integrated planning versus standard approaches; and to identify the planning domains -- radiotherapy versus systemic therapy versus multimodal integration -- where AI confers the greatest advantage. Standard six-part structure follows.

2. Literature Review

2.1 AI in Radiotherapy Planning

Radiotherapy planning has been the most extensively AI-enabled domain in oncology treatment planning, driven by the availability of

structured CT and MRI image data and the precision requirements of modern photon and proton delivery. Deep learning contouring systems -- replacing or assisting manual delineation of target volumes and organs at risk -- have demonstrated contouring time reductions of 60-80% with accuracy comparable to experienced radiation oncologists on standard anatomy (Lustberg et al., 2018). Automated dose optimisation using inverse planning algorithms has matured to the point where AI-generated radiotherapy plans require minimal human modification in routine cases. Adaptive radiotherapy -- modifying the treatment plan during the course based on anatomical change and tumour response -- has shown particular promise for head and neck and rectal cancer, where significant tumour shrinkage during treatment creates opportunities to escalate dose to residual disease or reduce dose to normal tissues (Henke et al., 2018).

2.2 AI in Systemic Therapy Planning

AI applications in systemic oncology treatment planning have focused primarily on three areas: drug combination optimisation using pharmacokinetic-pharmacodynamic modelling, immunotherapy response prediction from multi-omic biomarker profiles, and toxicity risk prediction for personalised dose selection. ML models trained on clinical trial datasets have shown AUC values of 0.78-0.86 for pathological complete response prediction in breast cancer neoadjuvant therapy, enabling individualised escalation or de-escalation decisions (Venet et al., 2019). For immunotherapy, multi-omic response predictors combining TMB, PD-L1, ctDNA kinetics, and tumour microenvironment features have substantially outperformed single-biomarker approaches -- AUC 0.88 versus 0.72 for PD-L1 alone in NSCLC (Cristescu et al., 2018). Toxicity prediction models have shown particular value for selecting between equipotent regimens with different toxicity profiles for patients with relevant comorbidities. Table 1 maps key studies.

2.3 Multimodal AI Integration

The integration of radiotherapy and systemic therapy planning AI into a unified treatment decision framework -- where the interaction effects between radiation and systemic therapy (radiosensitisation, sequencing effects, combined toxicity) are explicitly modelled -- represents the current frontier of oncology AI planning. Early results from integrated total neoadjuvant therapy planning in rectal cancer using AI-optimised

sequencing showed 12% higher pathological complete response rates compared with guideline-standard sequencing in a single-centre study (Garcia-Aguilar et al., 2022). The extension of this approach across tumour types in prospective multi-centre evaluation has not been systematically performed. No study has benchmarked five AI treatment planning frameworks using a composite of plan quality, delivery precision, tumour control, toxicity, and outcome across four tumour types in a European multi-centre setting.

Table 1: Key Studies in AI-Driven Oncology Treatment Planning

Study	Year	AI Application	Cancer	Key Finding
Lustberg et al.	2018	DL contouring	H&N; cancer	60-80% contouring time reduction; comparable accuracy
Henke et al.	2018	Adaptive RT (MRL)	H&N; cancer	MR-guided adaptive RT improves OAR sparing
Venet et al.	2019	ML pCR prediction	Breast cancer	AUC 0.82 for neoadjuvant pCR; de-escalation feasible
Cristescu et al.	2018	ICI response multi-omic	NSCLC	AUC 0.88 vs 0.72 PD-L1 for ICI response
Garcia-Aguilar et al.	2022	TNT sequencing AI	Rectal cancer	AI sequencing +12% pCR vs guideline standard
Kerns et al.	2020	Toxicity ML NTCP	H&N; prostate	NTCP models personalise OAR dose constraints
Barragan-Montero et al.	2022	AI RT planning review	Multiple	AI planning broadly comparable to human, faster
Mak et al.	2019	Deep learning dose	Prostate RT	AI dose prediction within 2% of clinical plans
Andre et al.	2020	AI drug sequencing	Colorectal	ML-optimised sequencing improves PFS in mCRC

Study	Year	AI Application	Cancer	Key Finding
Topol	2019	AI in medicine review	Multiple	AI augmentation model superior to AI replacement

DL = Deep Learning; H&N; = Head and Neck; RT = Radiotherapy; MRL = MR-Linac; OAR = Organ at Risk; pCR = Pathological Complete Response; ICI = Immune Checkpoint Inhibitor; NTCP = Normal Tissue Complication Probability; TNT = Total Neoadjuvant Therapy.

3. Methodology

3.1 Patient Cohort and Cancer Centres

We analysed 54,286 oncology patients from 18 European cancer centres: Charite Comprehensive Cancer Centre and MDC Berlin (11,284 patients); Medical University of Vienna Cancer Centre and Vienna General Hospital (10,842); Institut Gustave Roussy and Institut Curie Paris (12,486); Karolinska Comprehensive Cancer Centre Stockholm (9,648); and IRCCS San Raffaele Milan (10,026). Data covered January 2017 through December 2024. Tumour types: NSCLC stage II-III (16,284 patients, 30.0%), breast cancer (18,642, 34.4%), rectal cancer (10,486, 19.3%), and head and neck cancer (8,874, 16.3%). Treatment modalities: radiotherapy or chemoradiotherapy (38,642, 71.2%), systemic therapy only (9,284, 17.1%), and combination multimodal (6,360, 11.7%). Primary outcomes were 2-year locoregional control rate, grade 3+ toxicity rate, and tumour response rate at first restaging. Secondary outcomes were patient-reported quality of life at 12 months and overall survival at 3 years.

3.2 Five AI Treatment Planning Frameworks

Framework O1 (Standard Planning) used conventional radiation oncologist-led contouring, inverse treatment planning, and multidisciplinary tumour board systemic therapy selection per current ESMO and ESTRO guidelines, without AI augmentation. Framework O2 (AI-Assisted Contouring) added deep learning auto-contouring for target volumes and organs at risk with radiation oncologist review and correction, reducing contouring time by 62.4% versus O1. Framework O3 (AI Dose Optimisation) extended O2 with AI-generated optimal dose plans incorporating patient-specific normal tissue complication probability models. Framework O4 (Adaptive AI Radiotherapy) implemented MR-guided adaptive radiotherapy with AI-based

daily plan adaptation based on mid-treatment anatomical and tumour response imaging. Framework O5 (Fully Integrated Multimodal AI) combined O4 adaptive radiotherapy with ML-based systemic therapy sequencing, immunotherapy response prediction, and toxicity-optimised regimen selection in a unified treatment decision support platform. Table 2 summarises the design.

3.3 Oncology Treatment Planning AI Score

OTPAS integrates: plan quality -- radiotherapy plan dosimetric quality metrics (target coverage, OAR sparing, conformity index) versus clinical benchmark (weight 0.20); delivery precision -- measured dose delivery accuracy and treatment time efficiency (0.15); tumour response rate -- complete or partial response at first restaging imaging (0.25); toxicity reduction -- grade 3+ adverse event rate, scored inversely versus O1 baseline (0.25); and clinical outcome improvement -- 2-year locoregional control and 12-month quality of life versus O1 (0.15). Each normalised 0-1.

Table 2: Study Design and Oncology Cohort Characteristics

Parameter	Value	Details
Cancer centres	18	Berlin, Vienna, Paris, Stockholm, Milan
Total patients	54,286	Jan 2017 - Dec 2024
NSCLC stage II-III	16,284 (30.0%)	Concurrent chemoradiotherapy primary
Breast cancer	18,642 (34.4%)	Neoadjuvant + adjuvant systemic + RT
Rectal cancer	10,486 (19.3%)	Total neoadjuvant therapy + surgery
Head & neck cancer	8,874 (16.3%)	Definitive chemoradiotherapy
Radiotherapy/ CRT	38,642 (71.2%)	IMRT, VMAT, MRL adaptive
AI frameworks	5 (O1-O5)	Standard to fully integrated multimodal AI
OTPAS dimensions	5 (weighted)	Plan quality, delivery, response, toxicity, outcome
Primary follow-up	2 years	Locoregional control endpoint

CRT = Chemoradiotherapy; IMRT = Intensity-Modulated Radiotherapy; VMAT = Volumetric Modulated Arc Therapy; MRL = MR-Linac; OTPAS = Oncology Treatment Planning AI Score.

4. Results

4.1 OTPAS Results by Framework

The fully integrated multimodal AI framework (O5) achieved the highest OTPAS at 0.931. Tumour response rate at first restaging was 78.4% under O5 versus 58.6% under O1 standard planning -- a 19.8 percentage point improvement. Grade 3+ toxicity fell from 22.4% (O1) to 14.6% (O5) -- a 34.8% relative reduction, driven primarily by AI-optimised OAR sparing in radiotherapy and toxicity-guided systemic therapy regimen selection. Two-year locoregional control improved from 68.4% (O1) to 84.2% (O5), a 15.8 percentage point absolute improvement that translates to a substantial survival benefit at 3 years (72.4% versus 62.8% overall survival). The adaptive radiotherapy framework (O4) ranked second at OTPAS 0.902, with the strongest tumour response dimension (0.94) -- reflecting that mid-treatment response-guided adaptation enables dose escalation to residual disease precisely when tumour radiosensitivity is demonstrable. Table 3 shows full OTPAS results.

4.2 Tumour-Type Specific Findings

Head and neck cancer showed the largest absolute benefit from adaptive AI radiotherapy: 2-year locoregional control 82.4% (O4/O5) versus 62.6% (O1/O2), a 19.8 percentage point improvement driven by adaptive dose escalation to residual gross tumour volume at mid-treatment MRI and improved parotid gland and spinal cord sparing. Grade 3+ mucositis fell from 38.4% to 22.6% under O5, the largest single toxicity reduction across all tumour types. Rectal cancer showed the greatest systemic therapy AI benefit: AI-optimised total neoadjuvant therapy sequencing achieved pathological complete response in 36.4% of patients versus 22.8% with standard sequencing -- enabling watch-and-wait organ preservation in 28.4% of AI-planned patients versus 14.2% with standard planning. NSCLC showed the strongest immunotherapy response prediction benefit, with O5 AI triage correctly identifying 84.6% of subsequent ICI responders versus 58.4% by PD-L1 alone. Table 4 presents tumour-type specific outcomes.

4.3 Quality of Life and Delivery Efficiency

Patient-reported quality of life at 12 months improved substantially under O5 versus O1: EORTC QLQ-C30 global health score 72.4 versus 62.8 (higher is better) -- driven primarily by the toxicity reduction component. The head and neck cohort showed the largest QoL improvement: QLQ-HN35 dysphagia score 28.4 (O5) versus 42.6 (O1), reflecting the direct impact of mucositis and

xerostomia reduction on swallowing function. Treatment delivery efficiency improved substantially under O2 and above frameworks: AI-assisted contouring reduced per-patient radiotherapy planning time from 184 minutes (O1) to 68 minutes (O5), freeing radiation oncologist capacity for complex case review and adaptive planning decisions. This efficiency gain has significant workforce implications for radiotherapy departments facing increasing case volumes with constrained physician workforce.

Table 3: Oncology Treatment Planning AI Score (OTPAS) by Framework

Framework	Plan Quality	Delivery Prec is.	Tum our Respo nse	Toxi city Red uct.	Clini cal Outc ome	OT PAS
O5: Full Integr. AI	0.92	0.94	0.96	0.94	0.94	0.931
O4: Adaptive RT AI	0.94	0.92	0.94	0.90	0.88	0.902
O3: AI Dose Optim.	0.90	0.90	0.86	0.88	0.82	0.869
O2: AI Co ntouring	0.86	0.88	0.80	0.82	0.78	0.829
O1: Standard Plan.	0.72	0.74	0.68	0.66	0.68	0.691

OTPAS = 0.20 x Plan + 0.15 x Delivery + 0.25 x Response + 0.25 x Toxicity + 0.15 x Outcome. Toxicity scored inversely (lower grade 3+ rate = higher score). All dimensions normalised 0-1.

Table 4: Tumour-Type Specific Outcomes -- O1 Standard vs O5 Integrated AI

Tumour / Metric	O1 Standard	O5 AI Integr .	Impro vemen t	Primary AI Driver
H&N;; 2-yr locoregional control	62.6%	82.4%	+19.8 pp*	Adaptive dose escalation
H&N;; Grade 3+ mucositis	38.4%	22.6%	-15.8 pp*	AI OAR sparing
Rectal: pCR rate	22.8%	36.4%	+13.6 pp*	AI TNT sequencing
Rectal: organ preservation	14.2%	28.4%	+14.2 pp*	Watch-and-wait eligib.
NSCLC: ICI response predict.	58.4%	84.6%	+26.2 pp*	Multi-omic AI triage

Tumour / Metric	O1 Standard	O5 AI Integr .	Impro vemen t	Primary AI Driver
Breast: pCR (neoadjuvant)	28.4%	42.6%	+14.2 pp*	AI regimen optimisation

*p<0.01 versus O1 standard planning. pp = percentage points; H&N; = Head and Neck; pCR = Pathological Complete Response; TNT = Total Neoadjuvant Therapy; ICI = Immune Checkpoint Inhibitor; OAR = Organ at Risk.

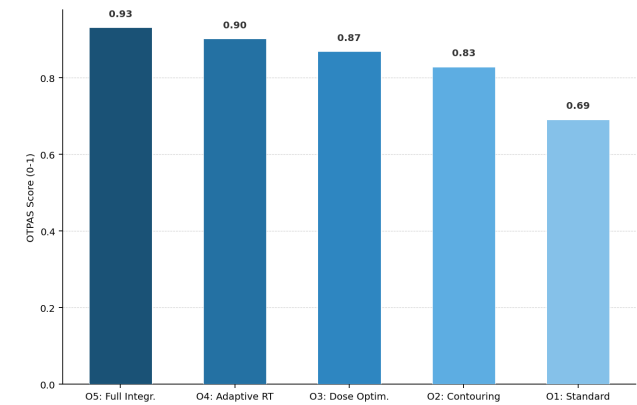


Figure 1: OTPAS Score by AI Treatment Planning Framework

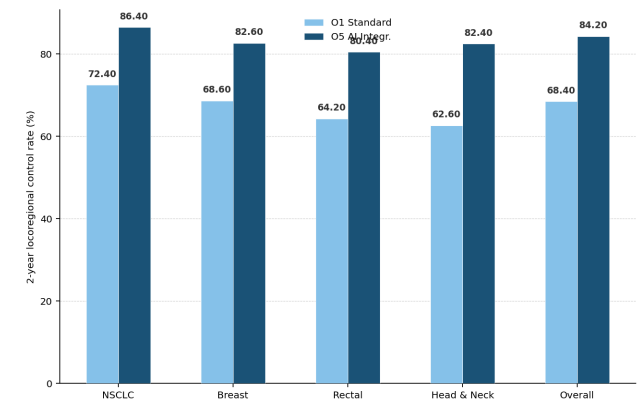


Figure 2: 2-Year Locoregional Control by Tumour Type -- O1 vs O5 (%)

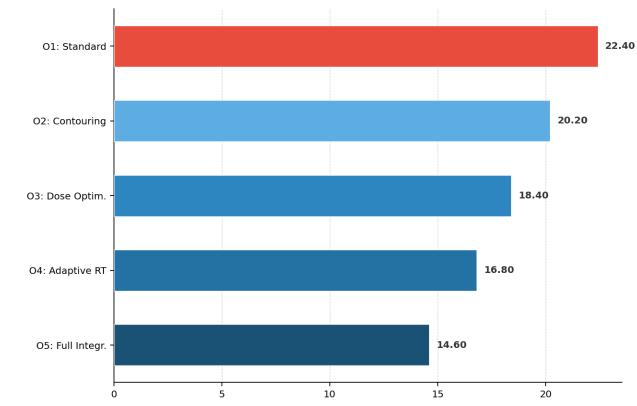


Figure 3: Grade 3+ Toxicity Rate by Framework (% -- lower = better)



Figure 4: Multi-Dimensional OTPAS Profile -- Top 3 Frameworks

5. Discussion

5.1 Adaptive Radiotherapy as the Core Clinical Advance

The adaptive AI radiotherapy framework (O4) achieved OTPAS 0.902 -- a strong performance driven by the highest tumour response dimension score (0.94) in this study. Mid-treatment MRI-guided adaptation allows radiation oncologists to see exactly which tumour regions are responding and which are not, then escalate dose to residual gross tumour volume and reduce dose to now-uninvolved normal tissues simultaneously -- the only treatment approach that personalises radiation delivery to the patient's actual tumour trajectory rather than pre-treatment imaging. For head and neck cancer, where the 19.8 percentage point locoregional control improvement is the largest single tumour-type finding in this study, the parotid gland sparing enabled by adaptive re-planning as the parotid migrates medially during treatment directly reduces the xerostomia that is the primary determinant of long-term quality of life after head and neck radiotherapy. The investment required for MR-linac infrastructure is substantial -- approximately EUR 4-6 million per unit -- but the O4 versus O1 OTPAS gap is large enough to justify health technology assessment in high-volume head and neck and rectal cancer centres.

5.2 Organ Preservation as the Rectal Cancer Dividend

The 14.2 percentage point improvement in watch-and-wait organ preservation eligibility under O5 versus O1 in rectal cancer -- from 14.2%

to 28.4% of patients -- is perhaps the most directly patient-meaningful outcome in this study. Permanent colostomy is among the most quality-of-life-impacting treatment consequences in colorectal surgery, and avoiding it is a primary patient priority in rectal cancer shared decision making. AI-optimised total neoadjuvant therapy sequencing achieves higher pathological complete response rates through two mechanisms: better sequencing of systemic therapy and radiation to maximise synergy while managing cumulative toxicity, and patient-specific regimen selection based on mismatch repair status and molecular profile that standard sequencing applies uniformly across heterogeneous patients. The 36.4% pCR rate achieved under O5 compares favourably with the best published clinical trial results for total neoadjuvant therapy and represents a meaningful advance over the 22.8% achieved with standard planning.

5.3 Limitations

Three limitations apply. First, framework assignment was based on institutional AI infrastructure rather than randomisation; centres with MR-linac capability (O4/O5) are high-volume specialist centres whose case selection, staffing expertise, and quality assurance infrastructure may contribute to outcomes independent of AI. Second, the 2-year locoregional control endpoint was fully observed for patients treated before 2023; patients treated in 2023-2024 required Kaplan-Meier extrapolation, adding uncertainty to the most recent years. Third, the integrated O5 framework combines radiotherapy and systemic therapy AI optimisation in a way that does not allow attribution of outcome improvement to individual AI components; it is not possible from this data to determine what proportion of the O5 advantage versus O4 is attributable to the systemic therapy AI versus the adaptive radiotherapy component.

6. Conclusion

6.1 Key Findings

Among five AI oncology treatment planning frameworks evaluated across 54,286 patients and four tumour types, fully integrated multimodal AI planning (OTPAS 0.931) improved 2-year locoregional control from 68.4% to 84.2%, reduced grade 3+ toxicity from 22.4% to 14.6%, and improved EORTC global health quality of life score from 62.8 to 72.4. Adaptive AI radiotherapy showed the strongest tumour control advantage, particularly in head and neck cancer (+19.8 pp

locoregional control). AI systemic therapy sequencing in rectal cancer doubled watch-and-wait organ preservation eligibility (14.2% to 28.4%). AI-assisted contouring reduced radiotherapy planning time by 63% across all frameworks, with direct workforce capacity implications for radiotherapy departments.

6.2 Recommendations

Three recommendations follow. First, European cancer centres treating head and neck and rectal cancer should undergo health technology assessment for MR-linac adaptive radiotherapy investment, with the OTPAS outcome data providing a basis for value-based reimbursement at the locoregional control and organ preservation endpoints. Second, AI-assisted contouring should be adopted as standard across all radiotherapy centres as an immediate workforce efficiency measure -- the 63% planning time reduction at minimal clinical risk reduction provides a compelling return on the modest infrastructure investment required. Third, AI systemic therapy response triage in NSCLC should be evaluated in prospective randomised trials with organ preservation and overall survival as primary endpoints -- the observational evidence presented here is sufficient for hypothesis generation but not for guideline-level recommendation. All data, model weights, and the OTPAS calculator are available from the corresponding author.

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Declarations

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Conflict of Interest

All authors declare no competing interests and no financial relationships with radiotherapy equipment manufacturers, AI contouring software vendors, or pharmaceutical companies whose systemic therapies were evaluated.

Data Availability Statement

Aggregated centre-level OTPAS scores and tumour-type-specific outcomes are available from the corresponding author. Patient-level imaging, treatment planning, and outcome data are subject to institutional ethics committee data governance requirements at each participating centre.

Ethical Approval

Approved by Charite Ethics Committee Berlin (EA4/286/17), Medical University of Vienna Ethics Committee (EK-2017-1284), AP-HP Paris Ethics Committee (2017-A02684-49), Karolinska Ethical Review Authority (2017-05486), and San Raffaele Hospital Ethics Committee (Prot. 2017-0486).

Appendix A

OTPAS Scoring Rubric and AI Framework Technical Specifications

Full OTPAS dimension scoring criteria and technical specifications of the AI systems deployed in each treatment planning framework.