

**Corso di dottorato: Intelligenza Artificiale In Medicina E Innovazione Nella Ricerca
Clinica E Metodologica**

Ciclo XXXIX

Imaging biomarker in head and neck cancer: a radiomics, delta radiomics study augmented with artificial intelligence and deep learning.

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Artificial Intelligence in Radiology

Artificial intelligence in radiology: decision support systems.

C E Kahn, Jr

Artificial Intelligence in Radiology

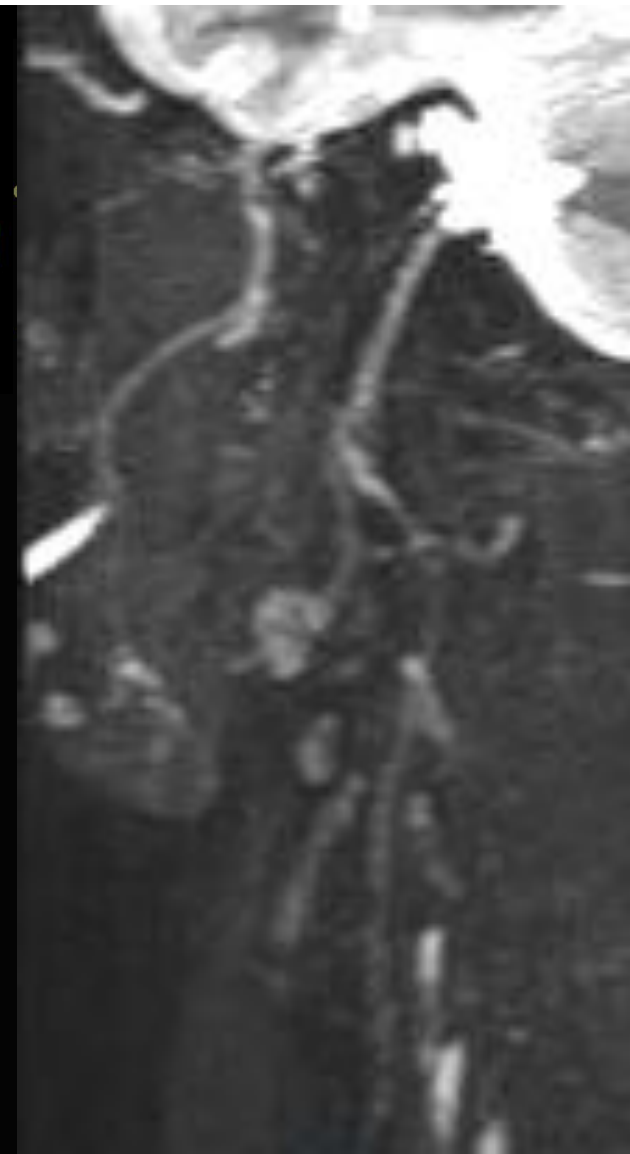
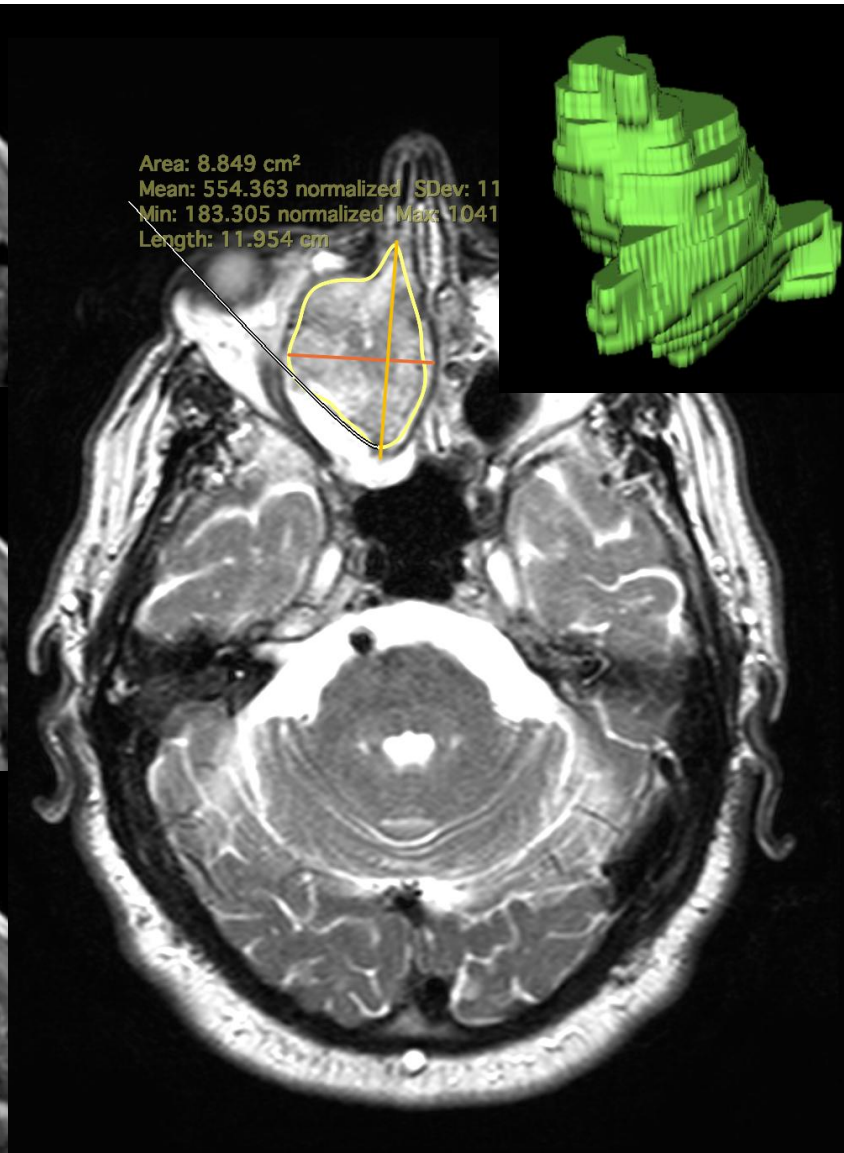
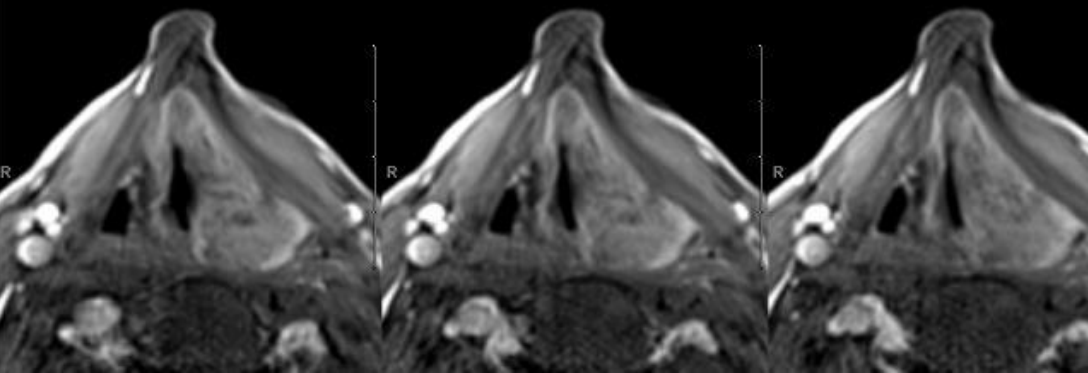
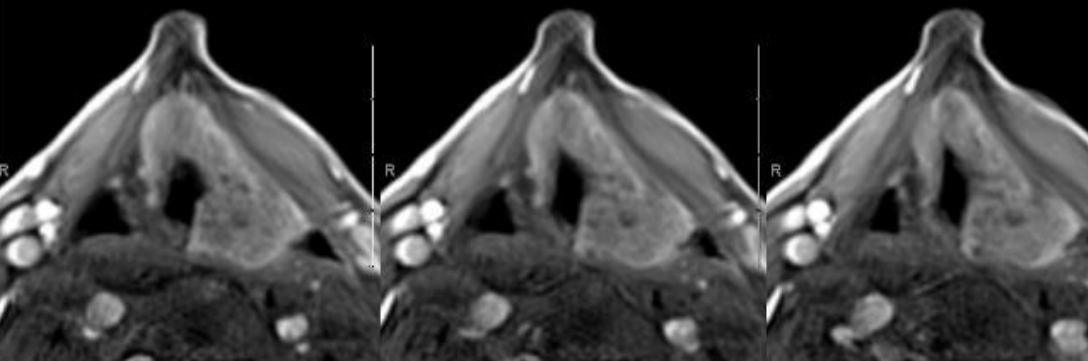
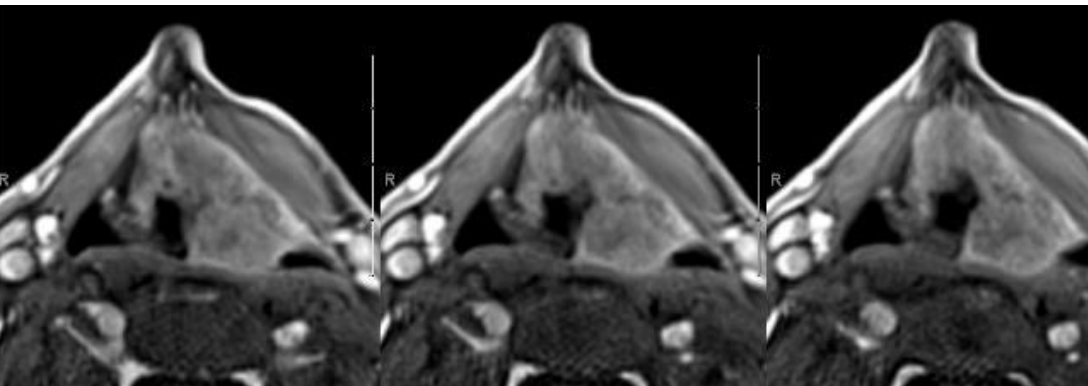
Artificial intelligence in radiology: decision support systems.

C E Kahn, Jr

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Artificial Intelligence in Radiology



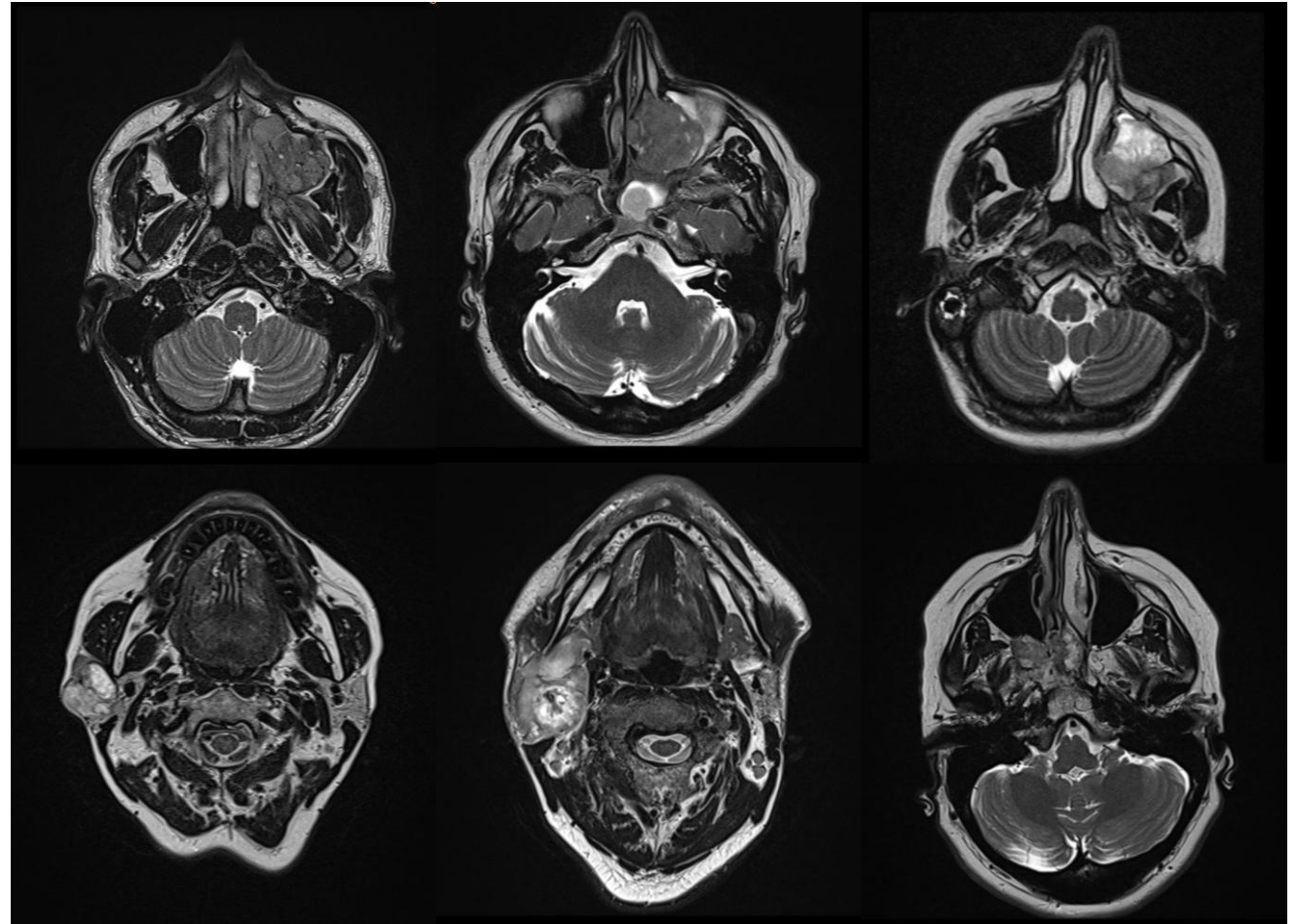
Aim of the project

The aim of this project is to **identify imaging biomarkers** with the help of AI and use them to **develop prognostic models**.

Head and neck cancers can arise from different histologies and show **highly variable prognoses**.

Even **within the same histology**, patients **may have very different outcomes**.

Identifying those with poorer prognosis is crucial to **personalize the diagnostic and therapeutic approach**.

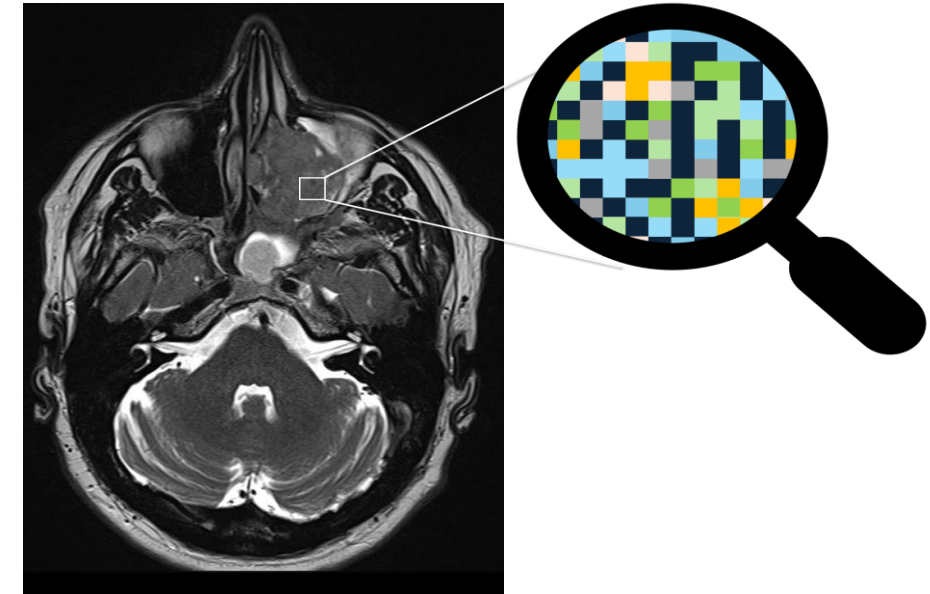


Introduction

Adenoid Cystic Carcinoma (AdCC) is a rare epithelial malignant tumor most commonly arising from the salivary glands.

AdCC incidence is **4.5 cases per 100.000** and it accounts for **1% of all head and neck cases**.

AdCC is slightly more common in females, with a median age at diagnosis in the 6th decade [1]. **Long-term prognosis is generally poor**, with 10-year survival estimates mostly ranging from 52% to 67% [2–4].



1. Ellington et al. Adenoid Cystic Carcinoma of the Head and Neck: Incidence and Survival Trends Based on 1973–2007 Surveillance, Epidemiology, and End Results Data. Cancer 2012, 118, 4444–4451.

2. Ciccolallo, L.; Licitra, L.; Cantù, G.; Gatta, G. EURO CARE Working Group Survival from Salivary Glands Adenoid Cystic

Carcinoma in European Populations. Oral Oncol. 2009,

3. Atallah et al. A Prospective Multicentre REFCOR Study of 470 Cases of Head and Neck Adenoid Cystic Carcinoma: Epidemiology and Prognostic Factors. Eur. J. Cancer 2020, 130, 241–249.

4. Terhaard, C.H.J. Dutch Head and Neck Oncology Cooperative Group Salivary Gland Carcinoma: Independent Prognostic Factors for Locoregional Control, Distant Metastases, and Overall Survival: Results of the Dutch Head and Neck Oncology Cooperative Group. Head Neck 2004, 26, 681–692.

Methods

A retrospective analysis of patients affected by primary salivary malignancies from 1995 to 2020 was conducted at the Department of Otolaryngology—Head and Neck Surgery, University of Brescia, Italy.

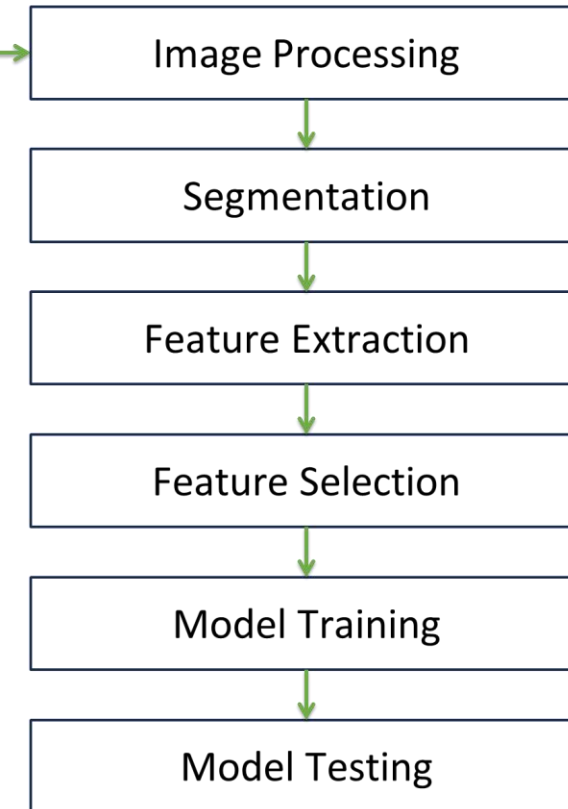
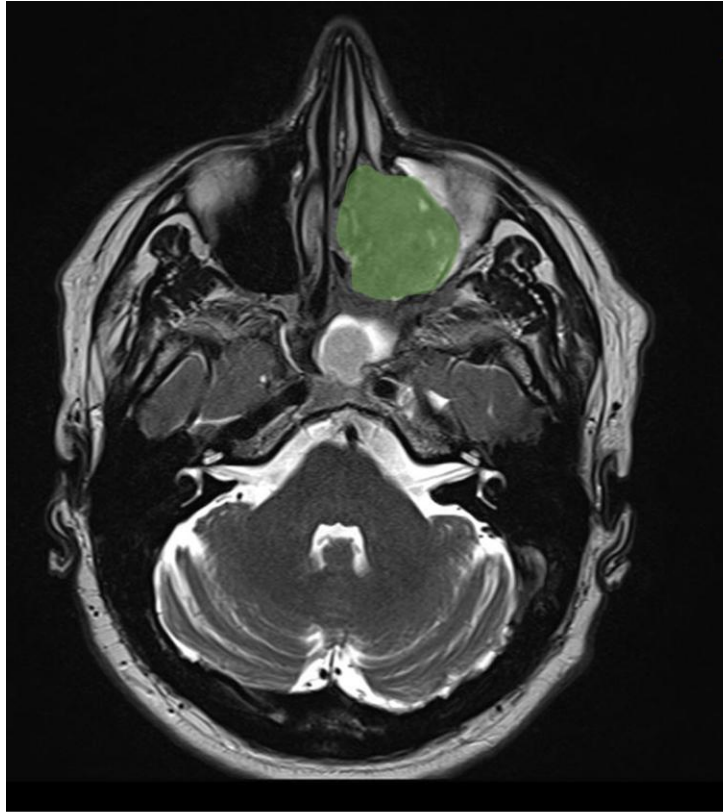
Inclusion criteria were:

- diagnosis of treatment-naive primary salivary gland AdCC;
- treated with upfront surgery with curative intent and adjuvant radiotherapy;
- availability of preoperative Magnetic Resonance Imaging (MRI) within one month prior to surgery (including turbo-spin-echo (TSE) T2-weighted sequences).

Exclusion criteria were:

- unavailability of adequate follow-up (at least 6 months after treatment);
- distant metastasis at diagnosis;
- inadequate image quality due to artifacts.

Image analysis



Statistical analysis

Using the Kaplan–Meier survival curves, the Relapse-Free Survival (RFS) probabilities were estimated at specific time points (up to 1 year, 3 years, and 5 years post-treatment).

The data were censored at these intervals to ensure an accurate representation of survival probabilities.

For identifying which of the clinical variables impact the outcome, namely the RFS, univariate Cox analysis was computed on the dataset, and variables with $p\text{-value} < 0.05$ were selected.

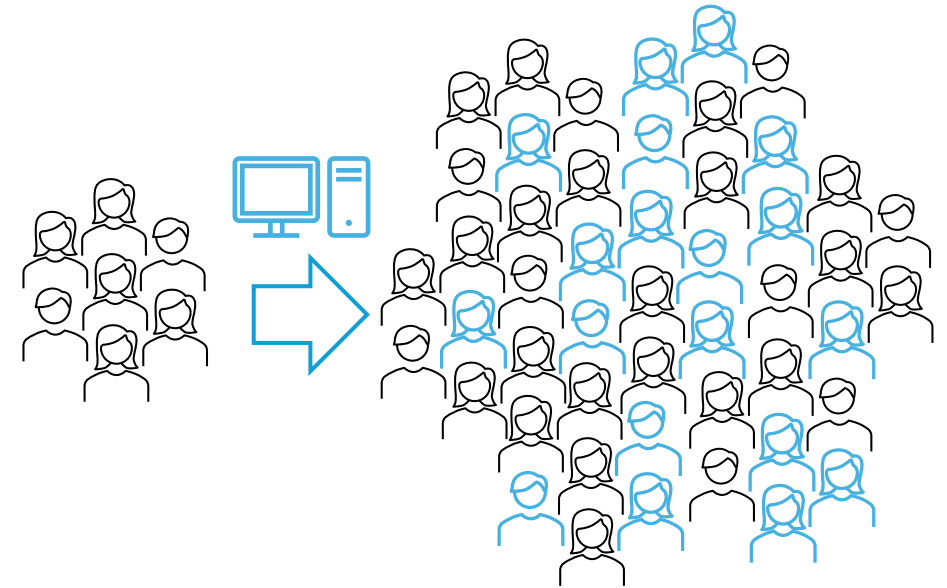
Since radiomics features, jointly with clinical variables, could increase the predictive accuracy of a survival model, a variable selection approach was used to identify those variables that have a strong impact on the RFS. In doing so, the Relative Variable Importance Measure (relVIM) extracted from the Survival Random Forest (SFR, which is a multivariate model) was used as a variable selection method for detecting which radiological features (covariates) predict the RFS (outcome).

Data augmentation

The **primary concern with multivariate analysis is the small sample size**, a **common situation in the presence of rare diseases**, which prevents splitting the observations into training and test sets. To extend the sample size, it is possible to use procedures that **increase observations of a real data set**.

They create artificial datasets that **mimic the statistical characteristics of real data and help to validate findings** from small patient cohorts, ensuring that conclusions drawn are not due to chance.

Data synthesis is developed using CART (Classification and Regression Trees), a non-parametric approach. However, for testing and validation purposes, it is crucial to use real data only. This approach ensures that the performance metrics obtained when estimating a model on synthetic data reflect the model's true capability to handle new, real-world data, and this keeps the evaluation honest and relevant.



Results

Three hundred and eighty consecutive patients affected by primary salivary malignancies were retrieved.

Among them, 104 were Adenoid Cystic Carcinoma.

Fifty-two patients met the selection criteria.

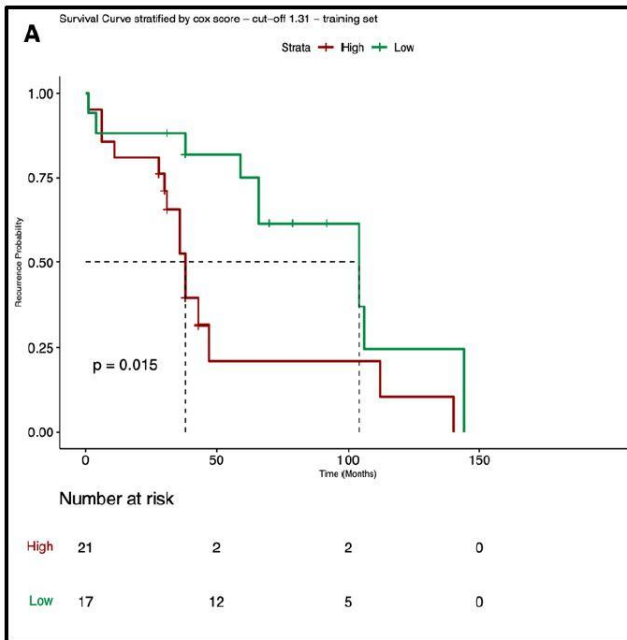
Table 1. Baseline patient and tumor characteristics.

Patients and Tumor Characteristics		
Gender	Female	63.5%
		Median age 53 (Inter-quartile range 38–61)
Site of origin	Minor salivary glands	79.6%
Subsite of origin	Sinonasal tract	44.9%
	Parotid gland	20.4%
	Oral cavity	18.4%
	Nasopharynx	10.2%
	Other	6.1%
Histologic grading according to Perzin–Szanto	High-grade (G3)	32.7%
	Intermediate-grade (G2)	49.0%
	Low-grade (G1)	18.3%
Tumor staging	pT1	6.1%
	pT2	8.2
	pT3	10.2%
	pT4	75.5%
Local tumor extension	Skin	6.1%
	Named nerves	58.3%
	Muscles	48.9%
	Bones	76.1%
	Cartilage	29.3%
Perineural invasion	Pn1	91.1%
Lymphovascular invasion	Lv1	24.4%
Surgical resection margins	R1	55.6%
	R2	15.6%
	N+	18.4%
N status	ENE+	14.3%
Extranodal extension		
Median N. of metastatic nodes (IQR)		2 (2–5)
Adjuvant treatment	RT	80.9%
	ChRT	14.9%

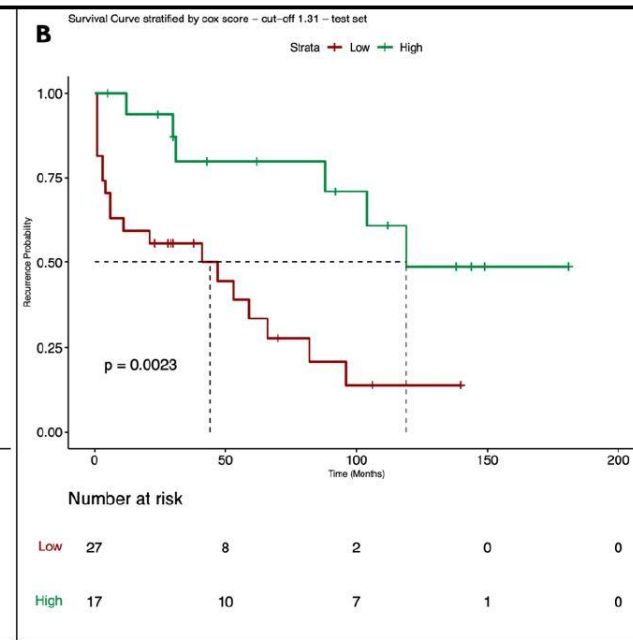
Results

Clinical model

Training Set

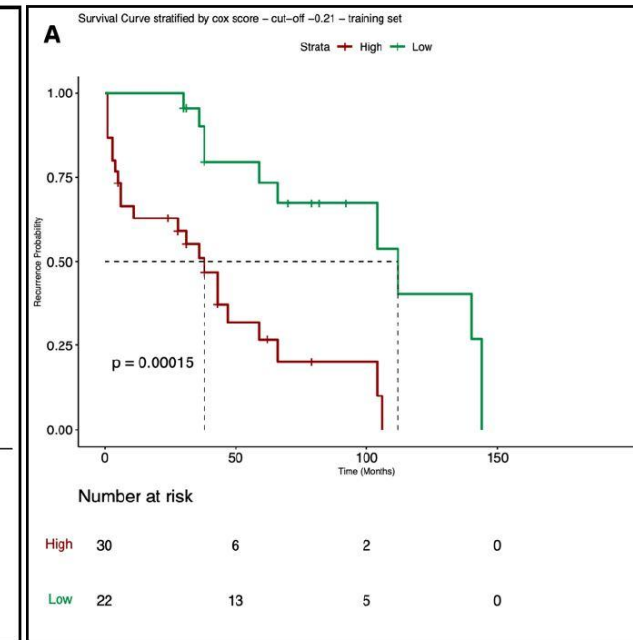


Validation Set

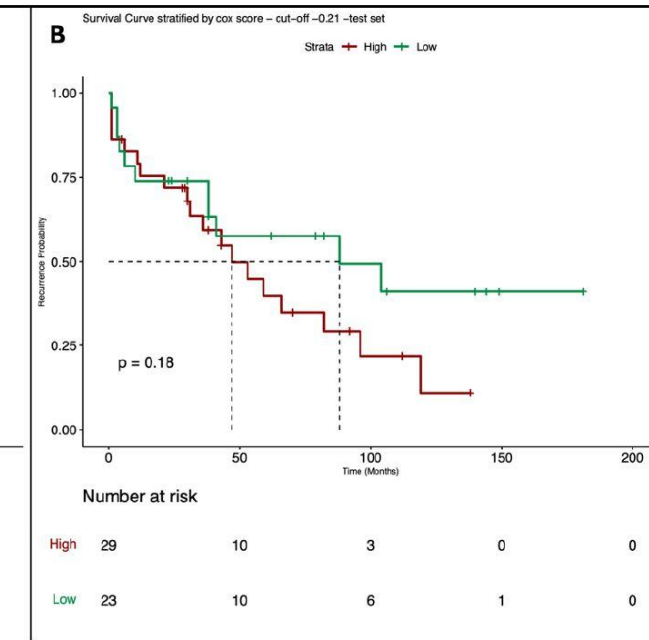


Radiomic model

Training Set



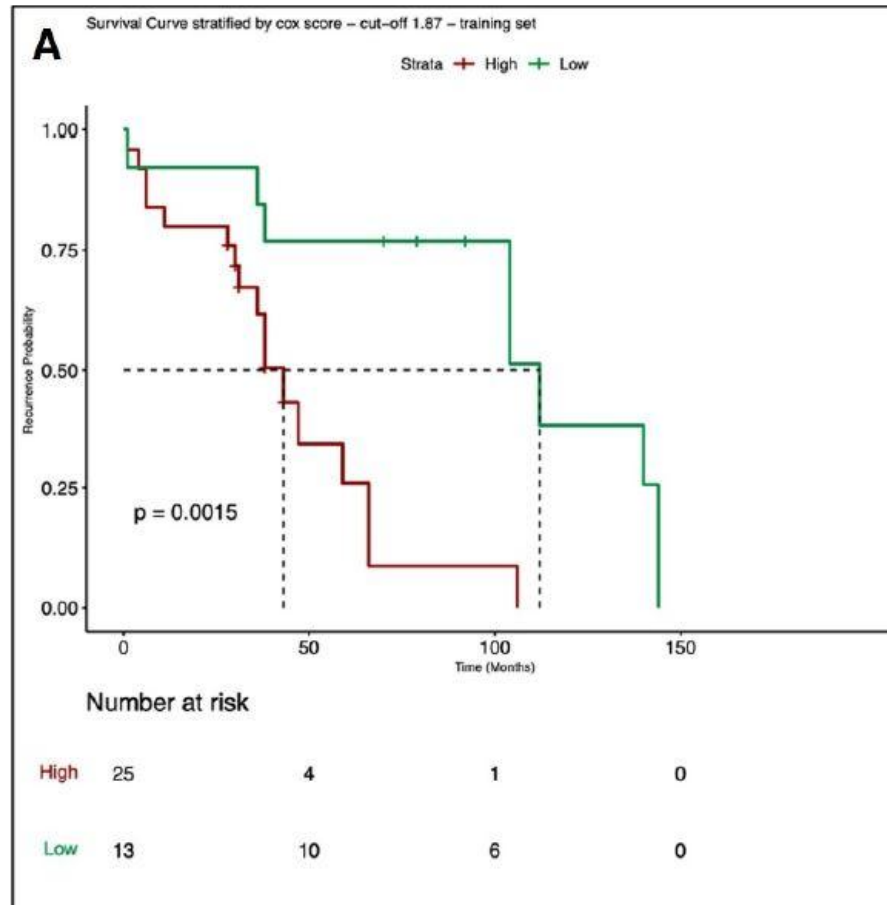
Validation Set



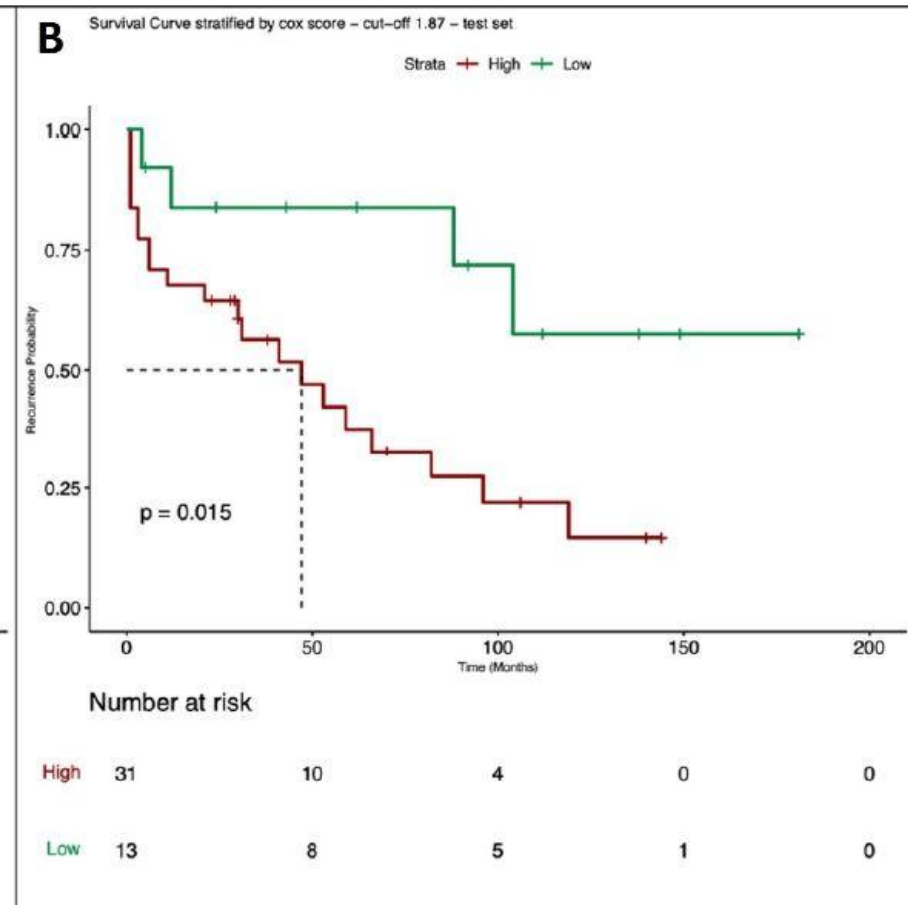
Results

Radiomic and Clinical model

Training Set



Validation Set



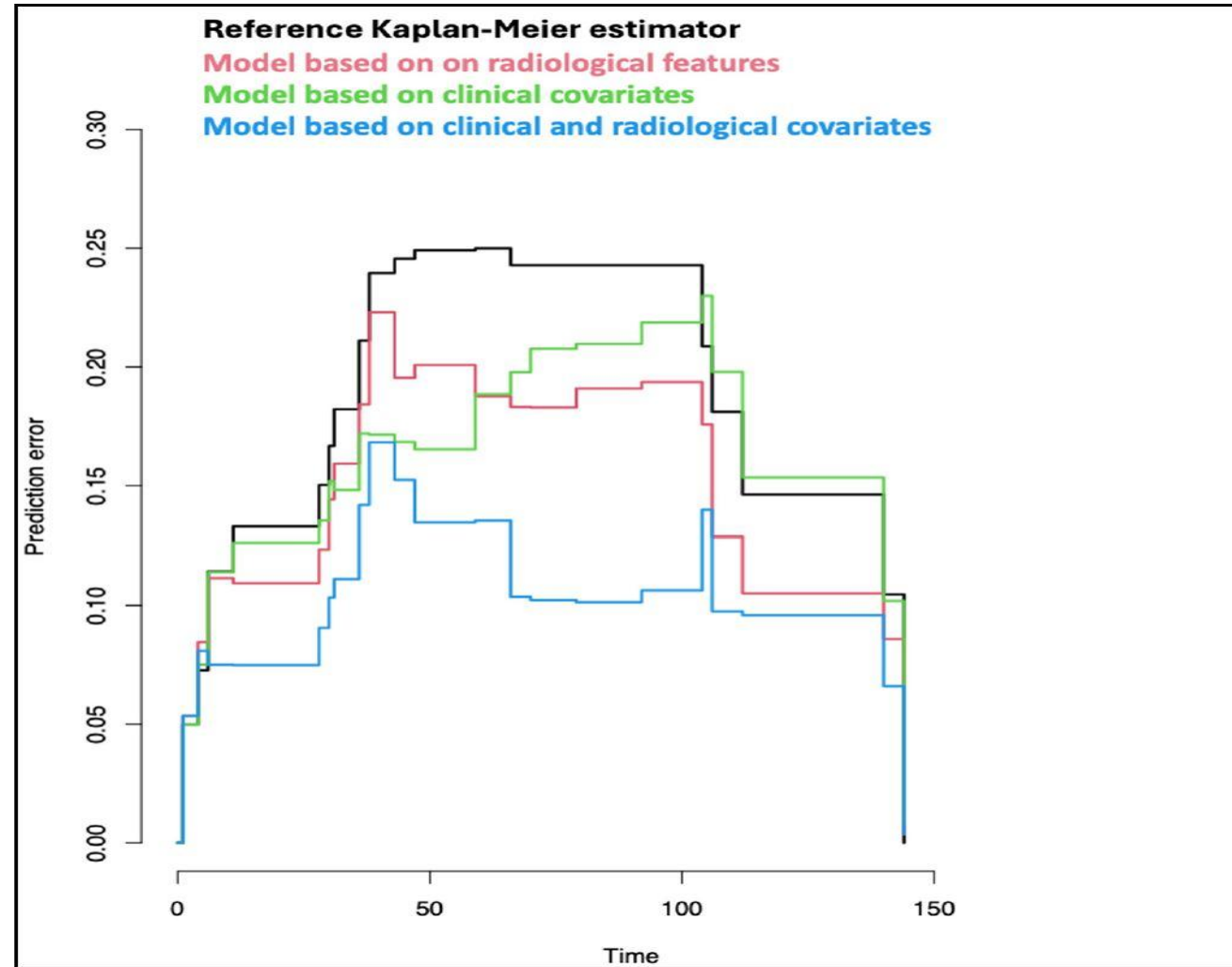
Model Selection

To select the best model among the three estimated, their performances were compared using the C-index.

The model with the highest C-index is that which is based on a combination of clinical and radiological covariates whose value (greater than 0.7) measures an optimal predictive ability.

Models	C-Index (se)
Model based on clinical covariates (grading and margin)	0.67 ± 0.07
Model based on radiological features (ten variables selected by SRF)	0.68 ± 0.04
Model based on clinical (grading and margin) and radiological (ten variables selected by SRF) covariates	0.77 ± 0.06

Prediction Error Curve



Conclusions

This study is the first to demonstrate the utility of a combined radiomic-clinical model to predict Relapse-Free Survival in AdCC patients.

The results obtained suggest that this model may provide clinicians with a valuable tool in the patient's management.

Accurate risk stratification is of great importance for treatment planning.

Article

Radiomic and Clinical Model in the Prognostic Evaluation of Adenoid Cystic Carcinoma of the Head and Neck

Paolo Rondi ^{1,*} , Michele Tomasoni ² , Bruno Cunha ³, Vittorio Rampinelli ², Paolo Bossi ^{4,5}, Andrea Guerini ⁶, Davide Lombardi ² , Andrea Borghesi ¹ , Stefano Maria Magrini ⁶ , Michela Buglione ⁶ , Davide Mattavelli ² , Cesare Piazza ², Marika Vezzoli ⁷ , Davide Farina ¹  and Marco Ravanelli ¹

Article

Fat Fraction Extracted from Whole-Body Magnetic Resonance (WB-MR) in Bone Metastatic Prostate Cancer: Intra- and Inter-Reader Agreement of Single-Slice and Volumetric Measurements

Giorgio Maria Agazzi ¹, Nunzia Di Meo ^{2,*}, Paolo Rondi ^{2,*}, Chiara Saeli ³, Alberto Dalla Volta ⁴, Marika Vezzoli ⁵, Alfredo Berruti ⁴, Andrea Borghesi ², Roberto Maroldi ², Marco Ravanelli ² and Davide Farina ²

Article

Magnetic Resonance Imaging after Nasopharyngeal Endoscopic Resection and Skull Base Reconstruction

Paolo Rondi ^{1,*}, Marco Ravanelli ^{1,*}, Vittorio Rampinelli ², Intan Zariza Hussain ³, Marco Ramanzin ¹, Nunzia Di Meo ¹, Andrea Borghesi ¹, Michele Tomasoni ², Alberto Schreiber ², Davide Mattavelli ², Cesare Piazza ² and Davide Farina ¹

The added value of radiomics in determining patient responsiveness to laryngeal preservation strategies

Marco Ravanelli, Paolo Rondi, Nunzia Di Meo and Davide Farina

Article

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Original Research Article

Adaptive radiotherapy for oropharyngeal cancer with daily adapt-to-shape workflow on 1.5 T MRI-linac: Preliminary outcomes and comparison with helical tomotherapy

Andrea Emanuele Guerini ^{a,*}, Michela Buglione ^{a,d,1}, Stefania Nici ^b, Stefano Riga ^b, Ludovica Pegurri ^c, Eneida Mataj ^c, Davide Farina ^c, Marco Ravanelli ^c, Paolo Rondi ^c, Gianluca Cossali ^d, Davide Tomasini ^e, Luca Triggiani ^e, Giorgio Facheris ^e, Luigi Spiazzi ^{b,d}, Stefano Maria Magrini ^{a,d}

Developments in the use of multiple imaging modalities for radiotherapy – Review

Adoption of Hybrid MRI-Linac Systems for the Treatment of Brain Tumors: A Systematic Review of the Current Literature Regarding Clinical and Technical Features

Andrea Emanuele Guerini, MD^{1,*}, Stefania Nici, BSc^{2,*}, Stefano Maria Magrini, MD¹, Stefano Riga, BSc², Cristian Toraci, PhD², Ludovica Pegurri, MD¹, Giorgio Facheris, MD¹, Claudia Cozzaglio, DEng^{1,2}, Davide Farina, MD³, Roberto Liserre, MD⁴, Roberto Gasparotti, MD⁵, Marco Ravanelli, MD³, Paolo Rondi, MD¹, Luigi Spiazzi, BSc^{2,†}, and Michela Buglione, MD^{1,†}

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Grazie per l'attenzione