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CT-based Radiogenomics of Neuroblastoma in predicting MYCN amplification

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IPOPORTO

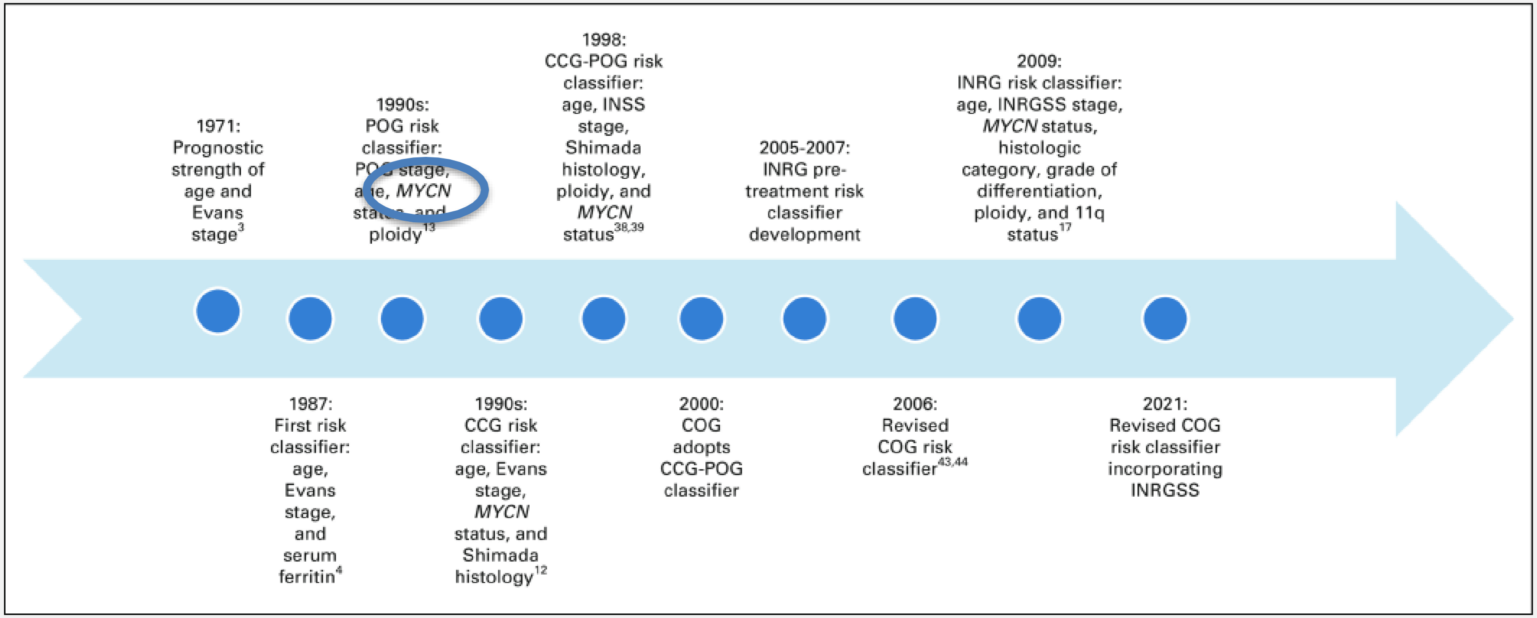
SÃO JOÃO

INESCTEC

Background

❑ Neuroblastoma (NB) is the most common extracranial tumor of childhood and a major cause of pediatric cancer related mortality

❑ Clinical heterogeneity is a hallmark of these tumors



Liang WH, Federico SM, London WB, et al. Tailoring Therapy for Children With Neuroblastoma on the Basis of Risk Group Classification: Past, Present, and Future. JCO Clin Cancer Inform. 2020;4:895-905

Background

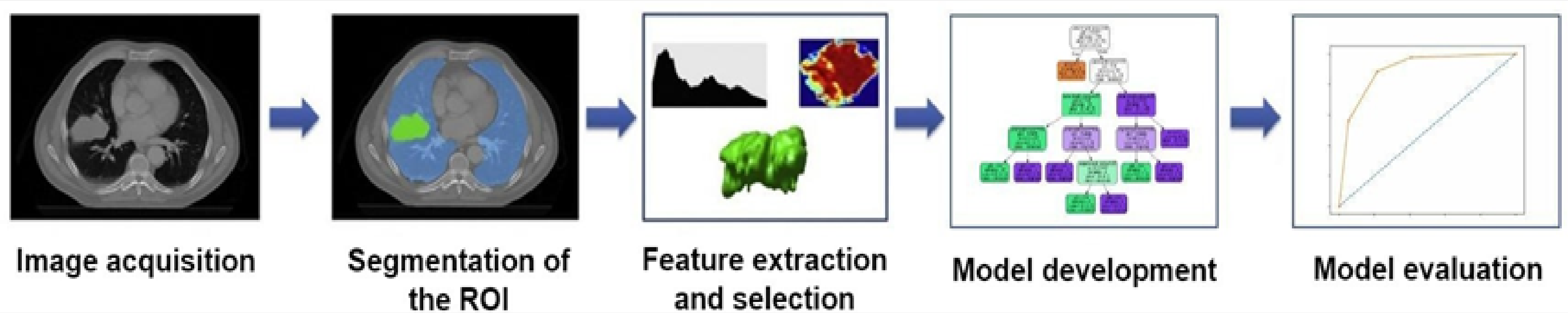
- MYCN belongs to the MYC transcription factor family and the presence of MYCN amplification (MNA) is an independent prognostic factor associated with rapid tumor progression and poor prognosis – high risk group
- MNA occurs in about 20% of patients
- MNA is generally detected by pathological examination of the tumor sample which is obtained by open or needle biopsy
    - MYCN status may be heterogenous throughout the tumor

Background

☐ As part of the workup for NB, a series of standard of care imaging studies are obtained either CT or MRI

☐ **Radiomics** is an emerging field involving the extraction and analysis of data from routine imaging studies

  ☐ Advanced image analysis that mathematically extracts a large number of quantitative features with the aid of specialized computer algorithms



Adapted from Lambin, Philippe et al. “Radiomics: extracting more information from medical images using advanced feature analysis.” European journal of cancer vol. 48,4 (2012): 441-6

☐ **Radiogenomics** incorporates genomic expression and radiomic data to produce diagnostic, predictive and prognostic models

Aim

- The aim of the present study was to evaluate the feasibility of CT based Radiogenomics analysis in NB pediatric patients, and its performance in predicting MNA expression of NB from standard staging CT scans
    - Predict individual risk assessment

Materials and Methods

- This was a double center retrospective study. Patients with NB were collected from the medical records of IPO-Porto and CHUSJ, Porto - Portugal
    - between 2005 and 2020
- Inclusion criteria:
    - Age under 18 years old at time of diagnosis
    - Histopathological confirmed neuroblastoma
    - MNA detection
    - Availability of multidetector CT studies at time of diagnosis before any intervention (biopsy, radiotherapy, chemotherapy or surgery)
- Data collection
    - gender, age at diagnosis, histopathological results and other genetic features associated with clinical behavior (ploidy and segmental chromosome alterations determination)

Materials and Methods

Image Analysis

- CT imaging data was retrieved from PACS and anonymized
    - 46 CT exams (33 CT with iv contrast)
- Reviewed by two pediatric radiologists blinded for the MNA status. Disagreements were resolved by discussion and consensus.

- Manual segmentation was performed on five representative cross-sectional images

Materials and Methods

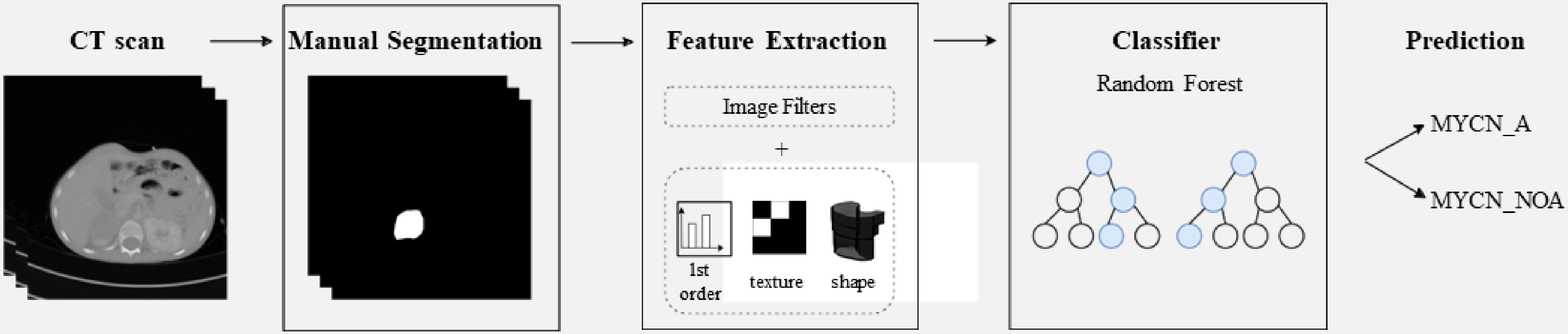
Radiomics analysis

Image processing and feature extraction

- An open source package *Pyradiomics* was used to extract 650 features from 2D ROIs (5 slices)

Training

- training set: 37 patients and test set: 9 patients



Pipeline developed for *MYCN* status prediction based on random forest classifier

Results and Discussion

❑Study cohort clinical characteristics

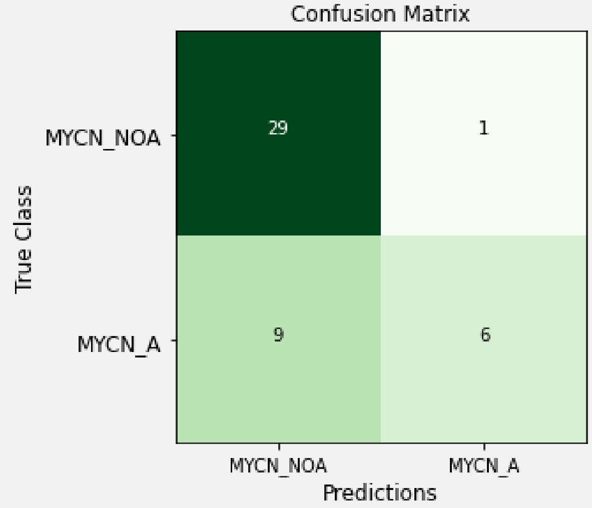
  - ❑45.7% male and 54.3% female
  - ❑Median age of 27 months (0 days to 87 months)
  - ❑MNA confirmed in 16 (34.8%)

Results and Discussion

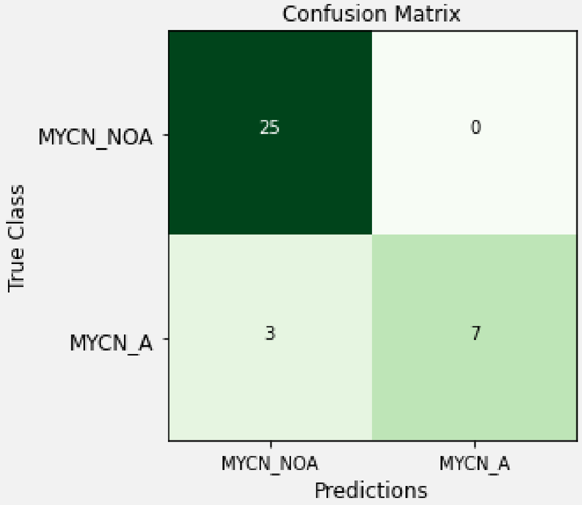
❑Radiomics analysis

- ❑*MYCN* Classification (Random Forest)

All patients



Contrast enhanced



	No of Patients	No of Slices (Train /Test)
Contrast	33	165 (130/35)
All	46	230 (185 / 45)

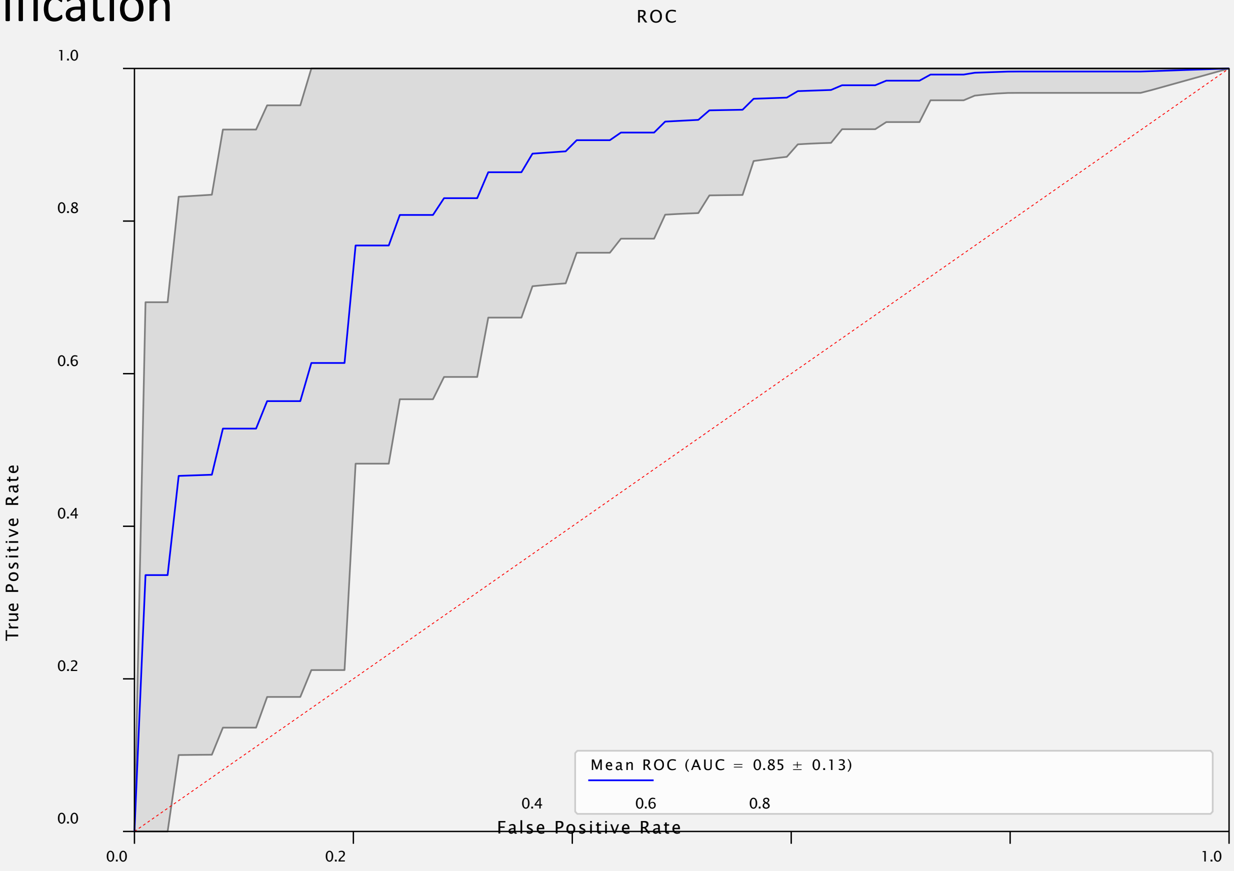
	AUC
Contrast	0.85 ± 0.13
All	0.69 ± 0.16

Results and Discussion

❑Radiomics analysis

❑*MYCN* Classification

AUC 0.85±0.13



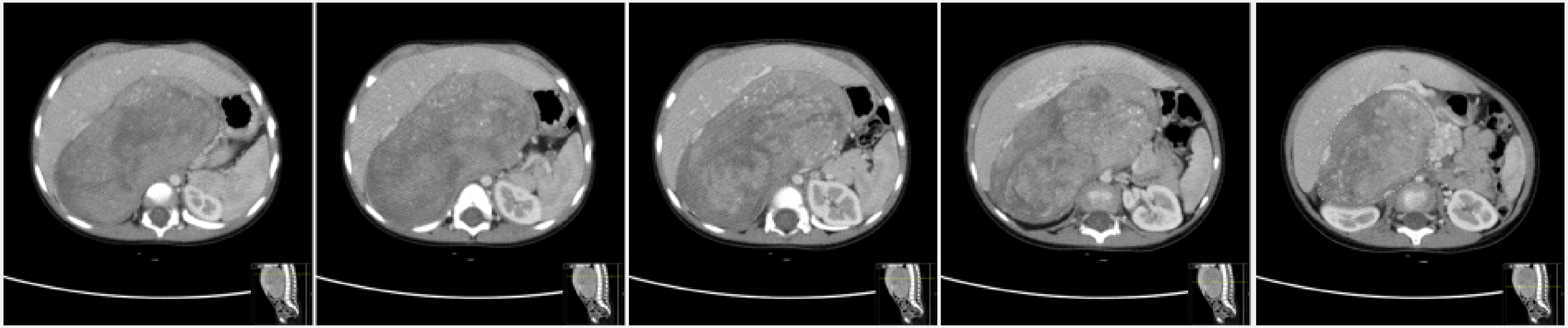
Wu H, Wu C, Zheng H, et al. Radiogenomics of neuroblastoma in pediatric patients: CT-based radiomics signature in predicting MYCN amplification. *Eur Radiol*. 2021;31(5):3080-3089

Chen, Xin, et al. "CT-Based Radiomics Signature With Machine Learning Predicts MYCN Amplification in Pediatric Abdominal Neuroblastoma." *Frontiers in oncology* 11 (2021): 1866.

Results and Discussion

- ❑ Radiomics analysis
  - ❑ Classification by Patient
    - ❑ Balanced accuracy results for MYCN amplification prediction by patient using a different number of positive slices to consider a positive patients

No of Slices	1	2	3	4	5
Contrast	0.74	0.73	0.75	0.75	0.76



    - ❑ 2D vs 3D

Di Giannatale, Angela, et al. "Radiogenomics prediction for MYCN amplification in neuroblastoma: A hypothesis generating study." *Pediatric Blood & Cancer* (2021)

Limitations

- Small size of the data set
    - deep learning-based methods need massive data to achieve a satisfactory generalization
    - Possible referral bias
- Heterogeneity of the data set
    - various scanners from different manufacturers and different institutions
    - contrast enhanced-CT and unenhanced-CT
- 2D Radiomics analysis
    - vs 3D segmentation

Conclusions

- The results obtained showed that information from radiomic features extracted from 2D segmentation of CT images allows to capture information relevant for MYCN amplification characterization.

Future challenges

- Prospective multicenter validation studies
- Nomogram that integrates clinical features
- Research for Radiogenomics in assessing other genomic risk predictors in neuroblastoma
    - DNA ploidy and chromosomal segmental alterations.

Acknowledgments

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  - CHUSJ - Centro Hospitalar e Universitário São João, Porto

Thank you for your attention