Radiogenomic integration in Radiation therapy and its impact - Review of evidence in Medulloblastoma

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DMG: Neuro oncology | Pediatrics | Hematolymphoid malignancies
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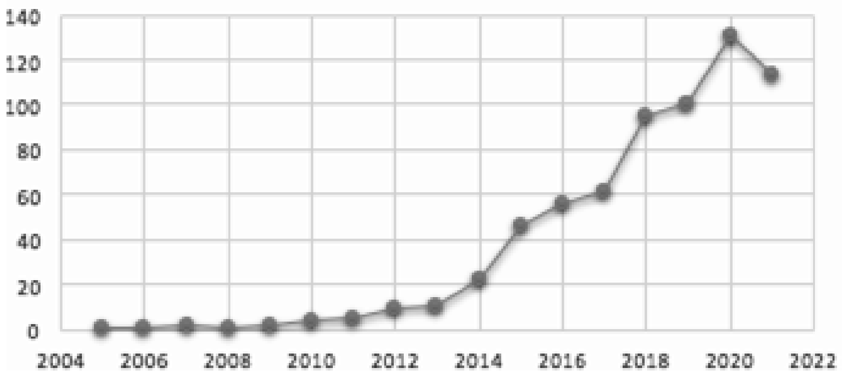
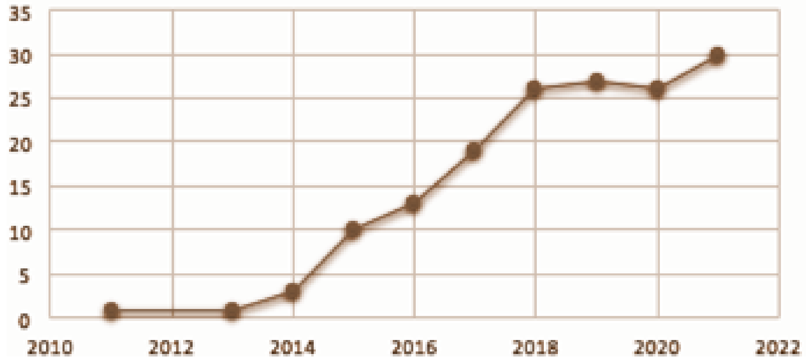
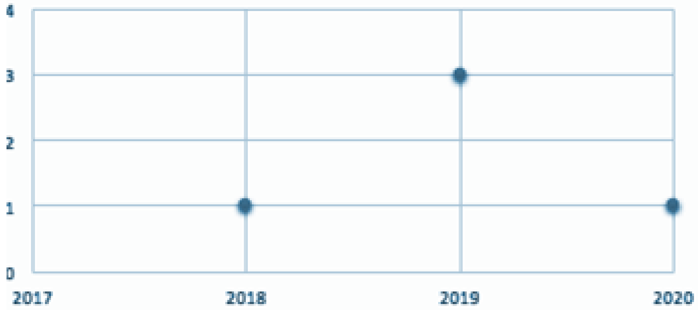
Radiogenomics - Pubmed Footprint
Radiogenomics | Brain | Medulloblastoma

Innovations in imaging transform nearly every aspect of healthcare - Horizons are just being known







Digital Medicine
Background thoughts - Radiomics | Radiogenomics

The idea of being able to probe disease characteristics rapidly and non-invasively - tremendously exciting!

Radiomics and radiogenomics - vast potential to improve clinical decision support systems, aid diagnosis, prognostic assessment, and treatment selection

Especially true when radiomic and radiogenomic data are processed using machine learning techniques

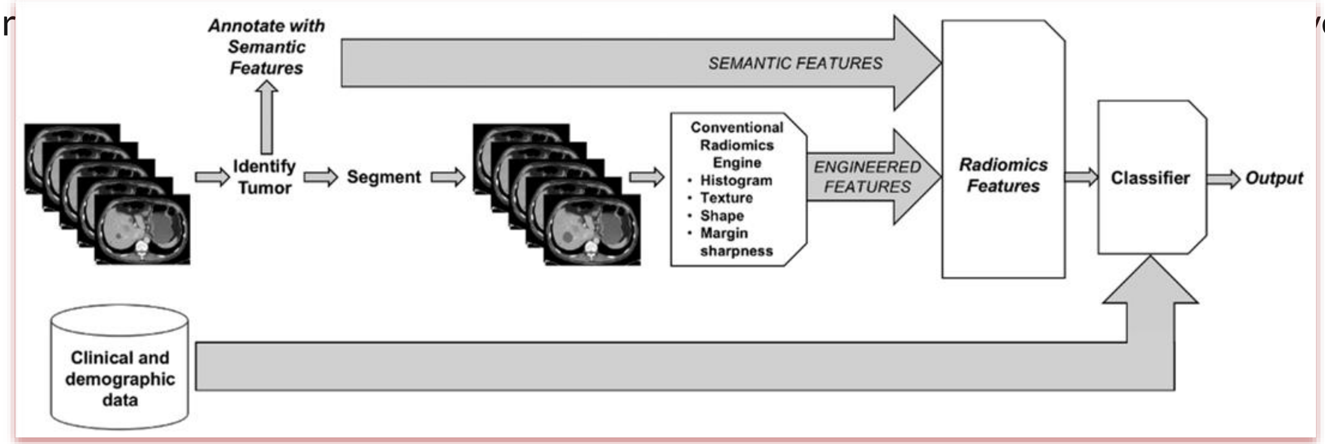
Analyze the features of entire tumors or other volumes of interest at any location and provide a picture of tissue heterogeneity within and across multiple volumes at a single time point

Particularly important for oncology, because tumor heterogeneity has been identified as a prognostic determinant of survival in different types of cancer, and an obstacle to cancer control

Radiomics | Radiogenomics
Definitions | Principles | Rationale

Radiomics - “High-throughput extraction of quantitative features that result in the conversion of images into mineable data” and feature prominently in what is today called “quantitative imaging”

Radiogenomics - The integration of radiomics with clinical data and the molecular char… …e models

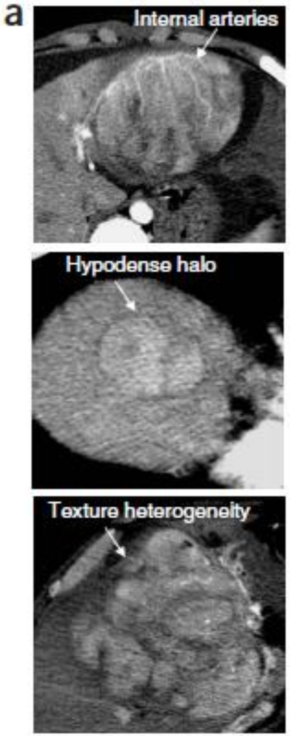


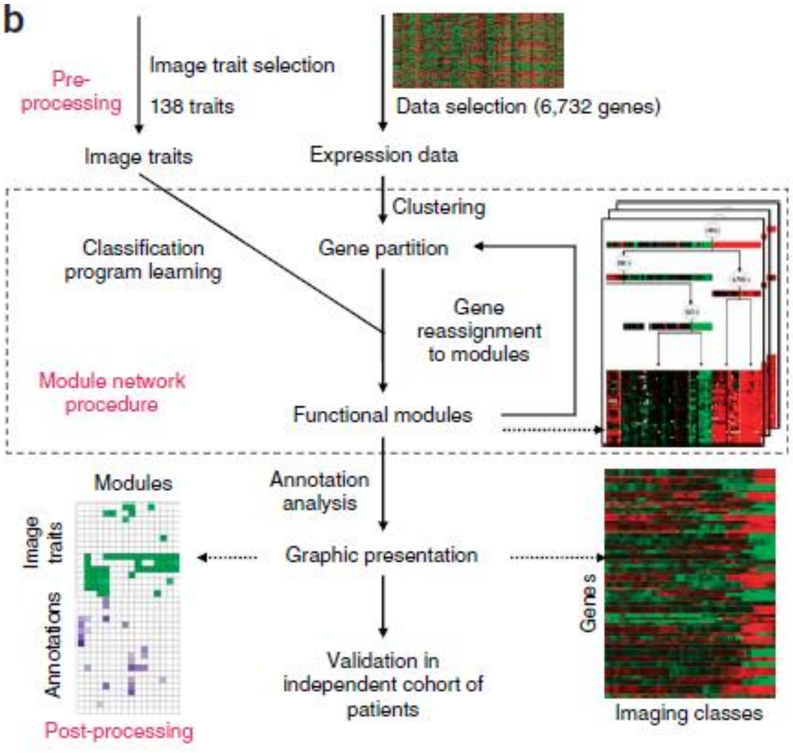
Hope of eventually contributing to clinical decision making, treatment management and through prognostic and predictive treatment response/ toxicity prediction models

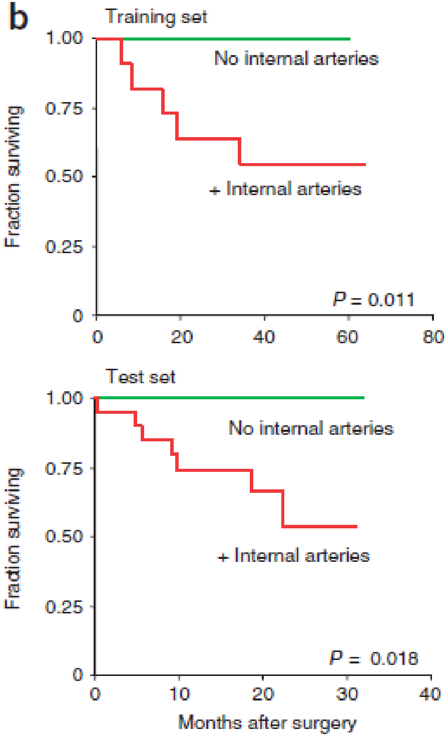
2007

Radiomics | Radiogenomics

Principles | Rationale - Early insights from liver cancer







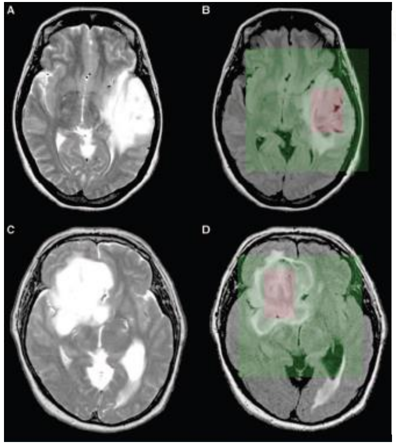
2008

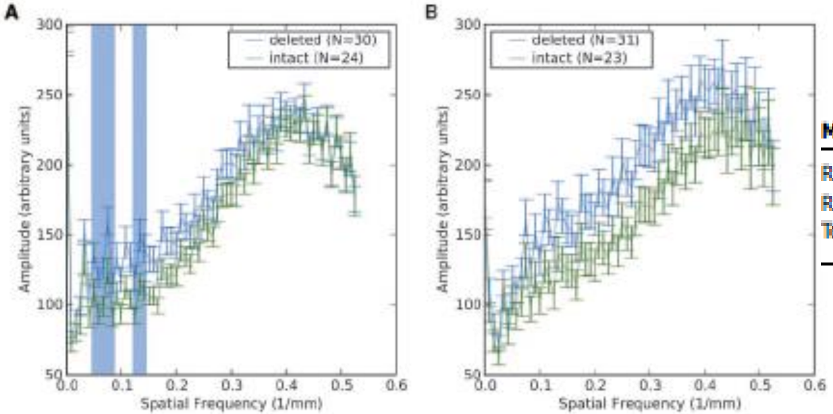
Radiomics | Radiogenomics

Principles | Rationale - Early insights from oligodendroglioma

The Use of Magnetic Resonance Imaging to Noninvasively Detect Genetic Signatures in Oligodendroglioma

Robert Brown,[1] Magdalena Zlatescu,[2,7] Angelique Sijben,[2] Gloria Roldan,[2,3] Jay Easaw,[3,7] Peter Forsyth,[3,7] Ian Parney,[2,7] Robert Sevick,[4,6,8] Elizabeth Yan,[3] Douglas Demetrick,[5] David Schiff,[9] Gregory Cairncross,[2,7,8] and Ross Mitchell[1,4,6,8]





1p19q detection from MR images

Method	Sensitivity	Specificity
Radiologist (Megyesi; ref. 4)	0.67	0.75
Radiologist (current study)	0.70	0.63
Texture analysis (current study)	0.93 ± 0.00061	0.96 ± 0.00048

Clin Cancer Res 2008;14(8) April 15, 2008

2011

Medulloblastomas epitomises the war against childhood cancer!

VOLUME 29 · NUMBER 11 · APRIL 10 2011

JOURNAL OF CLINICAL ONCOLOGY EDITORIALS

Hedgehogs, Flies, Wnts and MYCs: The Time Has Come for Many Things in Medulloblastoma

Michelle Monje, Philip A. Beachy, and Paul G. Fisher, *Stanford University, Palo Alto, CA*

- Overwhelming need for risk classification
  - Minimize unnecessarily aggressive therapy for low-risk disease
  - Maximize efficacious treatment for high-risk disease
- Four separate studies dovetailed with previous work
  - Crystallize a molecular classification of medulloblastoma
  - Codified a new risk-stratification model based on molecular biology of these disease subtypes

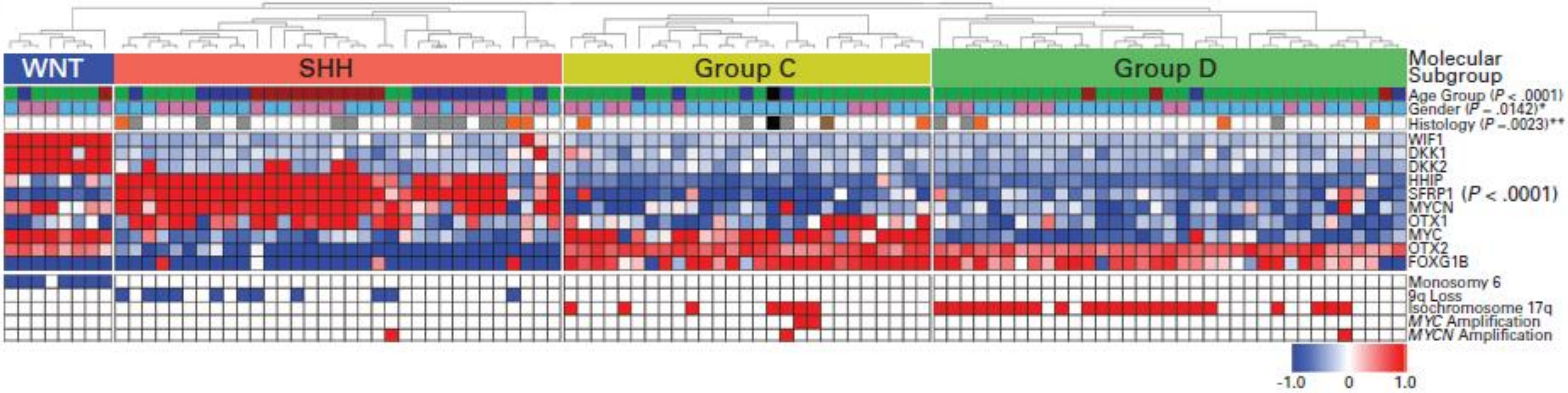
Radiomics | Radiogenomics

Medulloblastoma - Molecular subgroups

Medulloblastoma Comprises Four Distinct Molecular Variants

Paul A. Northcott, Andrey Korshunov, Hendrik Witt, Thomas Hielscher, Charles G. Eberhart, Stephen Mack, Eric Bouffet, Steven C. Clifford, Cynthia E. Hawkins, Pim French, James T. Rutka, Stefan Pfister, and Michael D. Taylor

A



J Clin Oncol 29:1408-1414. © 2010 by American Society of Clinical Oncology

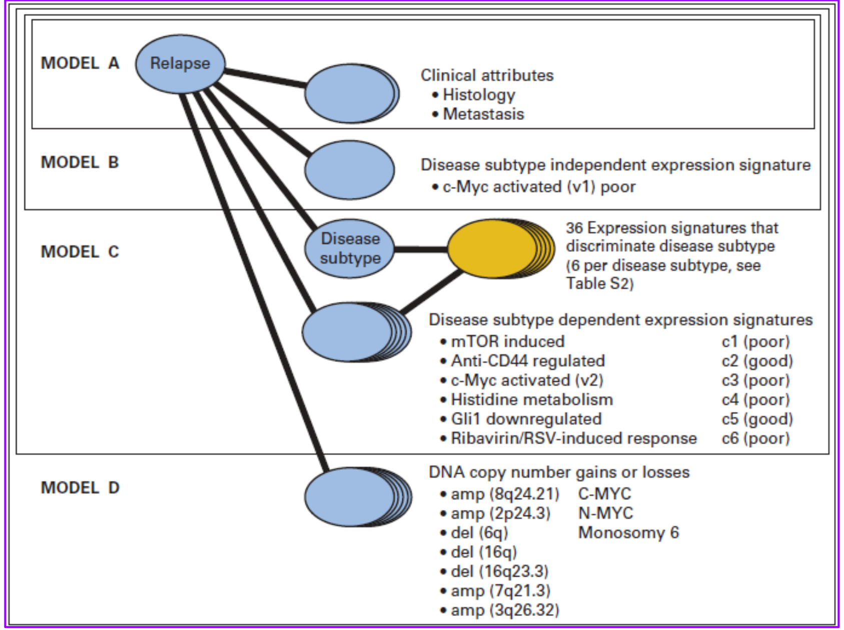
2011

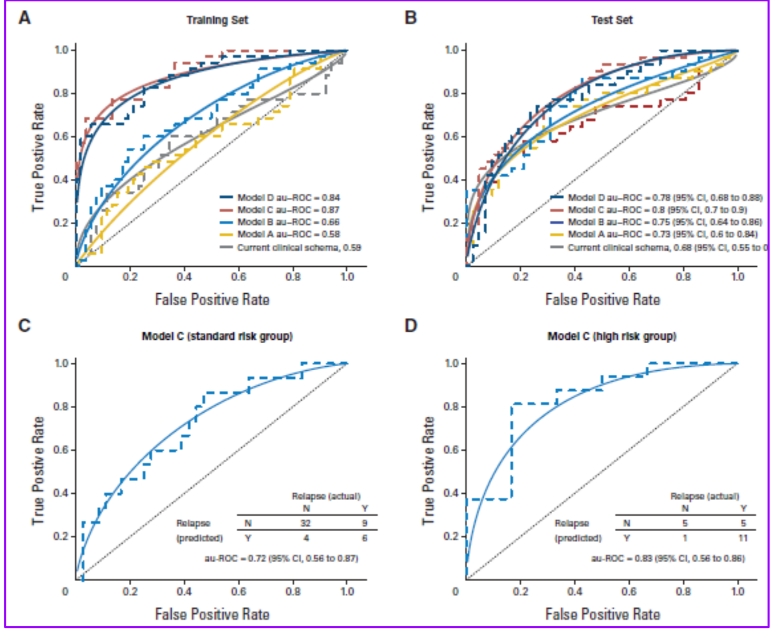
Predicting Relapse in Patients With Medulloblastoma by Integrating Evidence From Clinical and Genomic Features

VOLUME 29 · NUMBER 11 · APRIL 10 2011

JOURNAL OF CLINICAL ONCOLOGY

E D I T O R I A L S





2012

Radiomics | Radiogenomics

Decoding numbers!

NIH Public Access

Author Manuscript

Magn Reson Imaging. Author manuscript; available in PMC 2013 November 01.

Published in final edited form as:

Magn Reson Imaging. 2012 November ; 30(9): 1234–1248. doi:10.1016/j.mri.2012.06.010.

QIN "Radiomics: The Process and the Challenges"

Virendra Kumar[1], **Yuhua Gu**[1], **Satrajit Basu**[2], **Anders Berglund**[3], **Steven A. Eschrich**[3], **Matthew B. Schabath**[4], **Kenneth Forster**[5], **Hugo J.W.L. Aerts**[6,8], **Andre Dekker**[6], **David Fenstermacher**[3], **Dmitry B Goldgof**[2], **Lawrence O Hall**[2], **Philippe Lambin**[6], **Yoganand Balagurunathan**[1], **Robert A Gatenby**[7], and **Robert J Gillies**[*,1,7]

2012

Radiomics | Radiogenomics

Decoding numbers!



Image data → Image segmentation → Features extraction & qualification → Analysis and database

Image data
- Image modality
- Acquisition
- Reconstruction
- Image data storage

Image segmentation
- Ground truth
- Automate
- Reproducible
- Validate

Features extraction & qualification
- Features space
- Automatic extraction
- Informative
- Reproducible
- Low redundancy

Analysis and database
- Clinical and research PACS
- Storage & sharing of reports & annotations
- Integrations of clinical, imaging and genomics databases
- Informatics analyses

2014

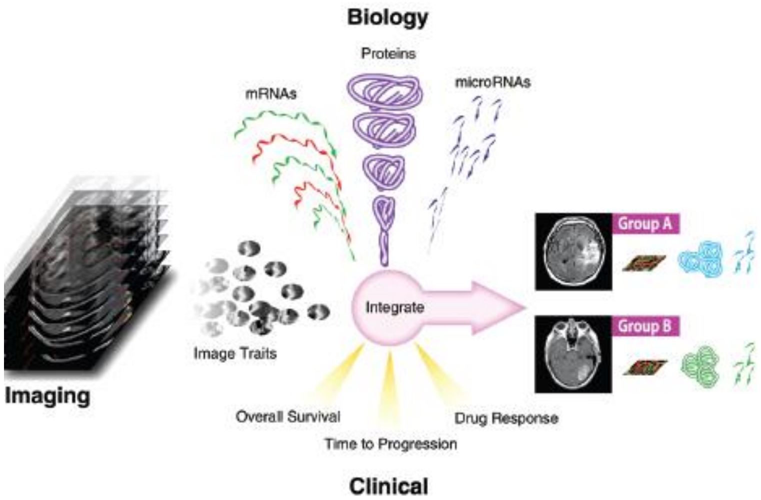
Radiomics | Radiogenomics

Decoding Molecular Phenotypes & Radiogenomics!

Michael D. Kuo, MD
Neema Jamshidi, MD, PhD

Behind the Numbers:
Decoding Molecular Phenotypes with Radiogenomics—Guiding Principles and Technical Considerations[1]

Radiology



- Understanding biological correlates behind imaging phenotypes
- Understanding how a biological process is reflected in imaging
- Defining clinical biomarkers or biological surrogates

radiology.rsna.org ▪ Radiology: Volume 270: Number 2—February 2014

2014

Radiomics | Radiogenomics

Radiogenomics - The Radiobiology Face!

REQUITE

Radiogenomics: Radiobiology Enters the Era of Big Data and Team Science

Barry S. Rosenstein, PhD[*,†,‡], Catharine M. West, PhD[§], Søren M. Bentzen, PhD, DSc[‖], Jan Alsner, PhD[¶], Christian Nicolaj Andreassen, MD[¶], David Azria, MD, PhD[#], Gillian C. Barnett,

Published in final edited form as:
Int J Radiat Oncol Biol Phys. 2014 July 15; 89(4): 709–713. doi:10.1016/j.ijrobp.2014.03.009.

- **Radiogenomics**
  - Study of the link between germ line genotypic variations and the large clinical variability observed in response to radiation therapy
- **Hypothesis**
  - Proportion of the variance in the phenotype of interest—radiation toxicity—is explained by genotypic variation

2016

2016, Annual Doppman Memorial Lecture, NIH
Professor Michael Kuo

Kuo and his team have pioneered the field of Radiogenomics
Help guide patient outcomes, and to predict treatment response

2013 - 2021

Radiomics | Radiogenomics

Medulloblastoma landscape - Correlates of imaging & molecular groups

Location features	Diffusion features	MRI-based nomograms for prediction of subgroups

2013 - 2021

Radiomics | Radiogenomics

Medulloblastoma landscape - Correlates of imaging & molecular groups

Location features	Teo (2013), perreault (2014), Wefers (2014), Lastowska (2015), Patay (2015), Zhao (2017), Mata-Mbemba (2018), Zapotocky (2018), Dasgupta (2018)

Dasgupta *et al*. *J Transl Genet Genom* 2018;2:15
DOI: 10.20517/jtgg.2018.21
Journal of Translational Genetics and Genomics

Review

Open Access

Check for updates

Radiogenomics of medulloblastoma: imaging surrogates of molecular biology

Archya Dasgupta, Tejpal Gupta

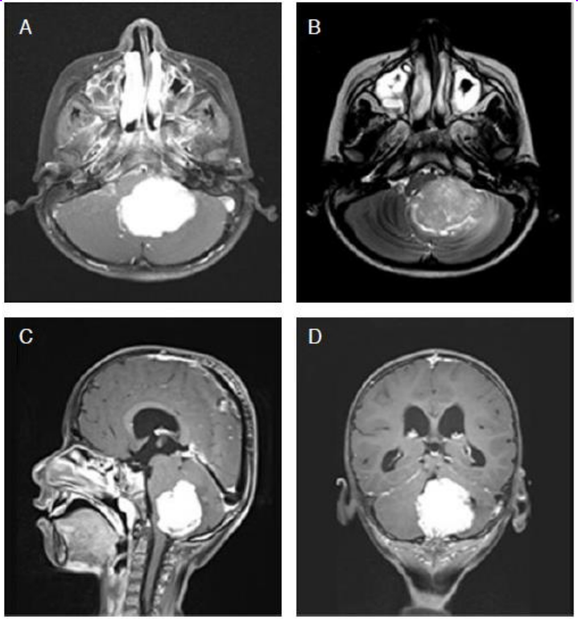
Location (horizontal axis)
Location (vertical axis)
Relation with dorsal brainstem
Contrast-enhancement
T2-weighted characteristics
Peri-tumoral edema
Intra-tumoral hemorrhage
Cyst (size and location)
Hydrocephalus
Metastases (incidence, location, and pattern)

Radiomics | Radiogenomics

WNT-MB landscape - Correlates of imaging & molecular groups

Location features	Teo (2013), perreault (2014), Wefers (2014), Lastowska (2015), Patay (2015), Zhao (2017), Mata-Mbemba (2018), Zapotocky (2018), Dasgupta (2018)

Location (horizontal axis) - Midline, CP/CPA
Location (vertical axis) - Central, inferior
Relation with dorsal brainstem - Infiltrate
Contrast-enhancement - homogeneous, bright
T2-weighted characteristics - Isointense, homogeneous
Peri-tumoral edema - Mild/ absent
Intra-tumoral hemorrhage - +/-
Cyst (size and location) - Intra-tumoral microcysts
Hydrocephalus - Absent/ mild
Metastases (incidence, location, and pattern) - Rare



Radiomics | Radiogenomics

SHH-MB landscape - Correlates of imaging & molecular groups

Location features	Teo (2013), perreault (2014), Wefers (2014), Lastowska (2015), Patay (2015), Zhao (2017), Mata-Mbemba (2018), Zapotocky (2018), Dasgupta (2018)

Location (horizontal axis) - Lateralised/ midline in infants

Location (vertical axis) - Superior abutting tentorium

Relation with dorsal brainstem - >50% away

Contrast-enhancement - Variable, moderate

T2-weighted characteristics - Isointense, heterogeneous

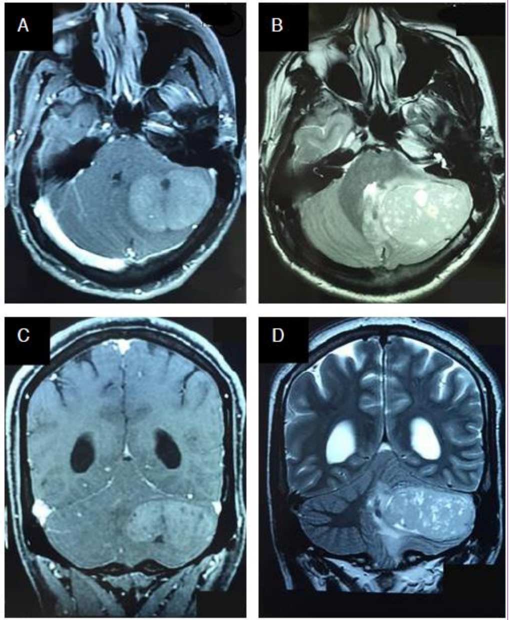
Peri-tumoral edema - Significant

Intra-tumoral hemorrhage - Absent

Cyst (size and location) - Intra- and peri-tumoral microcysts and macro

Hydrocephalus - Seldom

Metastases (incidence, location, and pattern) - Variable incidence

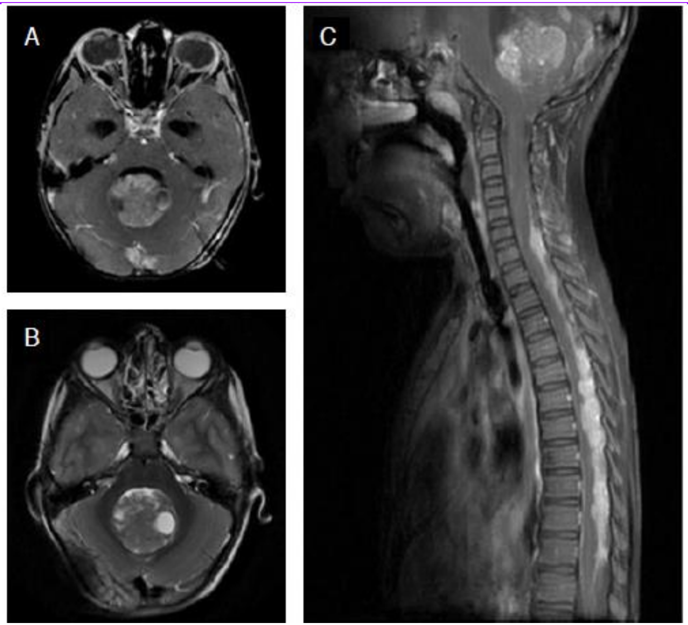


Radiomics | Radiogenomics

Group 3 MB landscape - Correlates of imaging & molecular groups

Location features	Teo (2013), perreault (2014), Wefers (2014), Lastowska (2015), Patay (2015), Zhao (2017), Mata-Mbemba (2018), Zapotocky (2018), Dasgupta (2018)

Location (horizontal axis) - Midline, 4th ventricle, vermis
Location (vertical axis) - Central
Relation with dorsal brainstem - Abuts
Contrast-enhancement - Heterogeneous, fluffy
T2-weighted characteristics - Hypointense, homogeneous
Peri-tumoral edema - Absent/ mild
Intra-tumoral hemorrhage - Absent
Cyst (size and location) - Peri-tumoral macrocysts
Hydrocephalus - Moderate to severe
Metastases (incidence, location, and pattern) - Highest



2013 - 2021

Radiomics | Radiogenomics

Group 4 MB landscape - Correlates of imaging & molecular groups

Location features	Teo (2013), perreault (2014), Wefers (2014), Lastowska (2015), Patay (2015), Zhao (2017), Mata-Mbemba (2018), Zapotocky (2018), Dasgupta (2018)

Location (horizontal axis) - Midline, 4th ventricle, vermis

Location (vertical axis) - Inferior

Relation with dorsal brainstem - Abuts

Contrast-enhancement - Heterogeneous, patchy

T2-weighted characteristics - Hyperintense, homogeneous

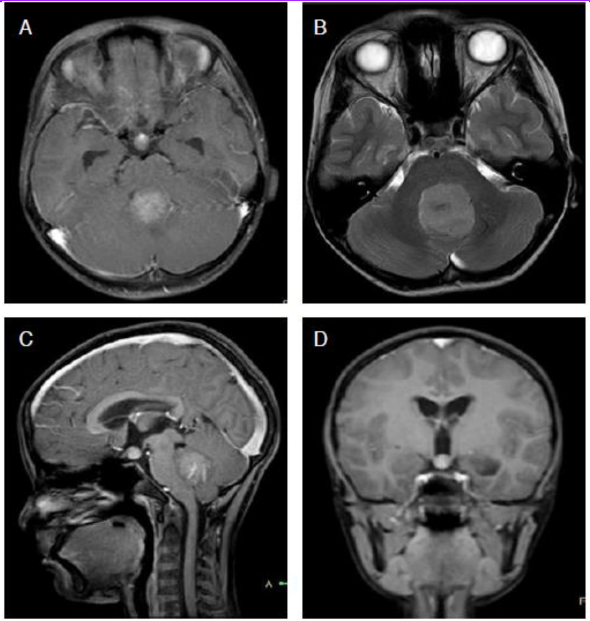
Peri-tumoral edema - Absent/ mild

Intra-tumoral hemorrhage - Absent

Cyst (size and location) - Intra-tumoral microcysts

Hydrocephalus - Moderate to severe

Metastases (incidence, location, and pattern) - Moderate



Medulloblastoma - Correlates of diffusion & molecular groups

Diffusion features	Mata-Mbemba (2018), Zapotocky (2018)
Group 4 MB	Ependymal metastasis with restricted diffusion but no enhancement “Mismatch pattern” Particularly if located in the infundibular recess

2018, 2021

Radiomics | Radiogenomics

Medulloblastoma - MRI based nomograms, predictive models, prognosticators for subgroups

Models	Dasgupta (2018), Chang (2021)

Neuro-Oncology
21(1), 115–124, 2019 | doi:10.1093/neuonc/noy093 | Advance Access 29 May 2018

Nomograms based on preoperative multiparametric magnetic resonance imaging for prediction of molecular subgrouping in medulloblastoma: results from a radiogenomics study of 111 patients

Archya Dasgupta, Tejpal Gupta, Sona Pungavkar, Neelam Shirsat, Sridhar Epari, Girish Chinnaswamy, Abhishek Mahajan, Amit Janu, Aliasgar Moiyadi, Sadhana Kannan, Rahul Krishnatry, Goda Jayant Sastri, and Rakesh Jalali

Table 3 Area under the curve (AUC) with 95% CI) of receiver operating characteristics (ROC) curves for subgroup-specific nomograms in the training cohort and validation cohort

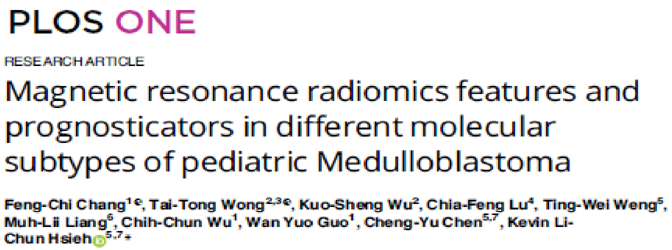
Molecular Subgroup	AUC (95% CI)in Training Cohort ($n = 76$)	AUC (95% CI)in Validation Cohort ($n = 35$)
WNT	0.754 (0.624–0.885)	0.693 (0.416–0.970)
SHH	0.939 (0.887–0.991)	0.991 (0.971–1.000)
Group 3	0.726 (0.582–0.870)	0.600 (0.380–0.820)
Group 4	0.851 (0.733–0.969)	0.788 (0.632–0.945)

2018, 2021

Radiomics | Radiogenomics

Medulloblastoma - MRI based nomograms, predictive models, prognosticators for subgroups

Models	Dasgupta (2018), Chang (2021)

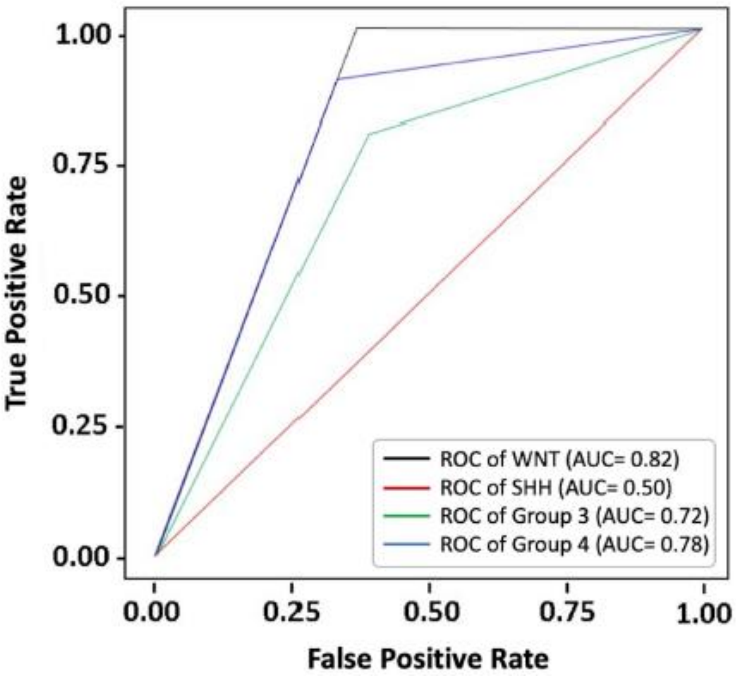

PLOS ONE

RESEARCH ARTICLE

Magnetic resonance radiomics features and prognosticators in different molecular subtypes of pediatric Medulloblastoma

Feng-Chi Chang[1©], Tai-Tong Wong[2,3©], Kuo-Sheng Wu[2], Chia-Feng Lu[4], Ting-Wei Weng[5], Muh-Lii Liang[6], Chih-Chun Wu[1], Wan Yuo Guo[1], Cheng-Yu Chen[5,7], Kevin Li-Chun Hsieh[5,7*]

- 8 contrast-enhanced T1-weighted texture features were significantly different between 4 molecular subgroups
- Together with prediction models, the radiomics features may provide suggestions for stratifying patients with MB into different risk groups



2007 - 2021

Radiomics | Radiogenomics

Medulloblastoma - Quest for non invasive markers & the essentials to build a radiogenomics model

- Discover non-invasive biomarkers that mirror the molecular properties of these tumors
- Most clinically used biomarkers use a piece of tissue and apply genomics
- Subtyping of medulloblastoma is often based on gene expression of 22 genes - nanostring
- Knowing the subtype of informs on the biology of the disease and what treatment is likely to help
- Main disadvantage is that surgical sampling - invasive
- Biomarkers on imaging - potentially more easy to implement?
- Quantitative imaging is a great candidate to investigate whether feature(s) can serve as a biomarker for the underlying biological type
- Add to this - toxicity prediction
- Becomes a heady cocktail of personalised treatment with some knowledge of outcomes & toxicity
- Essentials to build the model - coordination of experts to integrate
    - The genomics strategy
    - Quantitative imaging strategy
    - The integration strategy

Summary