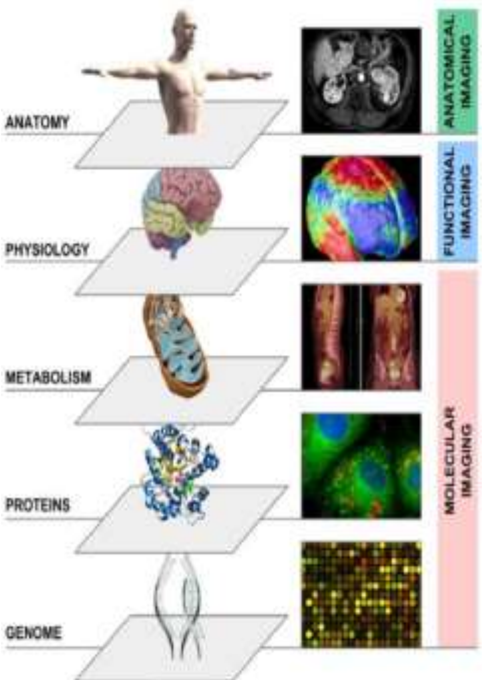
Associazione Italiana di Oncologia Medica

POST- ESMO: From Barcelona to real world

NH Collection Vittorio Veneto - Corso D'Italia, 1

Roma 2-3 Dicembre 2019



Radiomica tra presente e futuro

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Radiology
Regina Elena National Cancer Institute
Rome Italy

Modulo dichiarazione conflitto di interessi

Tutti i rapporti finanziari intercorsi negli ultimi due anni devono essere dichiarati.

☒ Non ho rapporti (finanziari o di altro tipo) con le Aziende del farmaco

☐ Ho / ho avuto rapporti (finanziari o di altro tipo) con le Aziende del farmaco

Relationship	**Company/Organization**

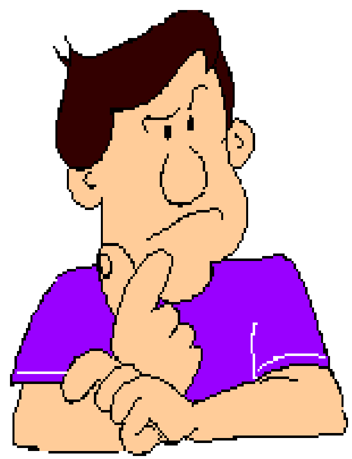
radiomics

radiogenomics

deep learning

machine learning

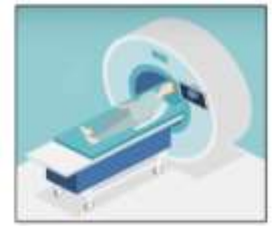
artificial intelligence



cancer patients

cancer imaging

- US / CT/ MR / PET-CT



biomedical images

- *contain information that reflects underlying pathophysiology and that these relationships can be revealed via quantitative image analyses*

combining data

- *patient characteristics*

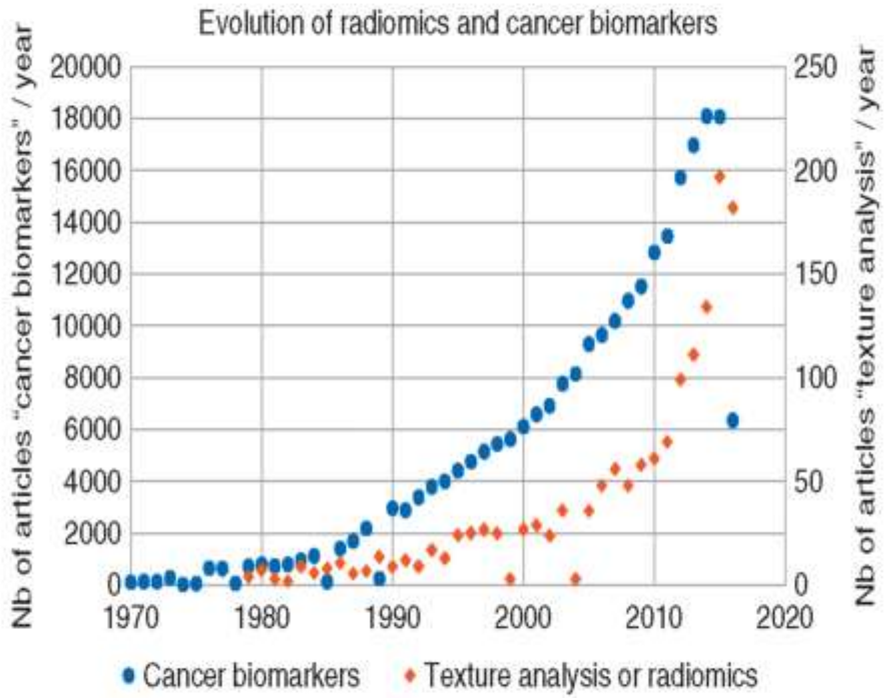
develop support tool

Radiomics

Radio + Omics

genomics (DNA) - transcriptomics (RNA)
proteomics - metabolomics

is simply the extraction of a high number of quantitative features from medical images



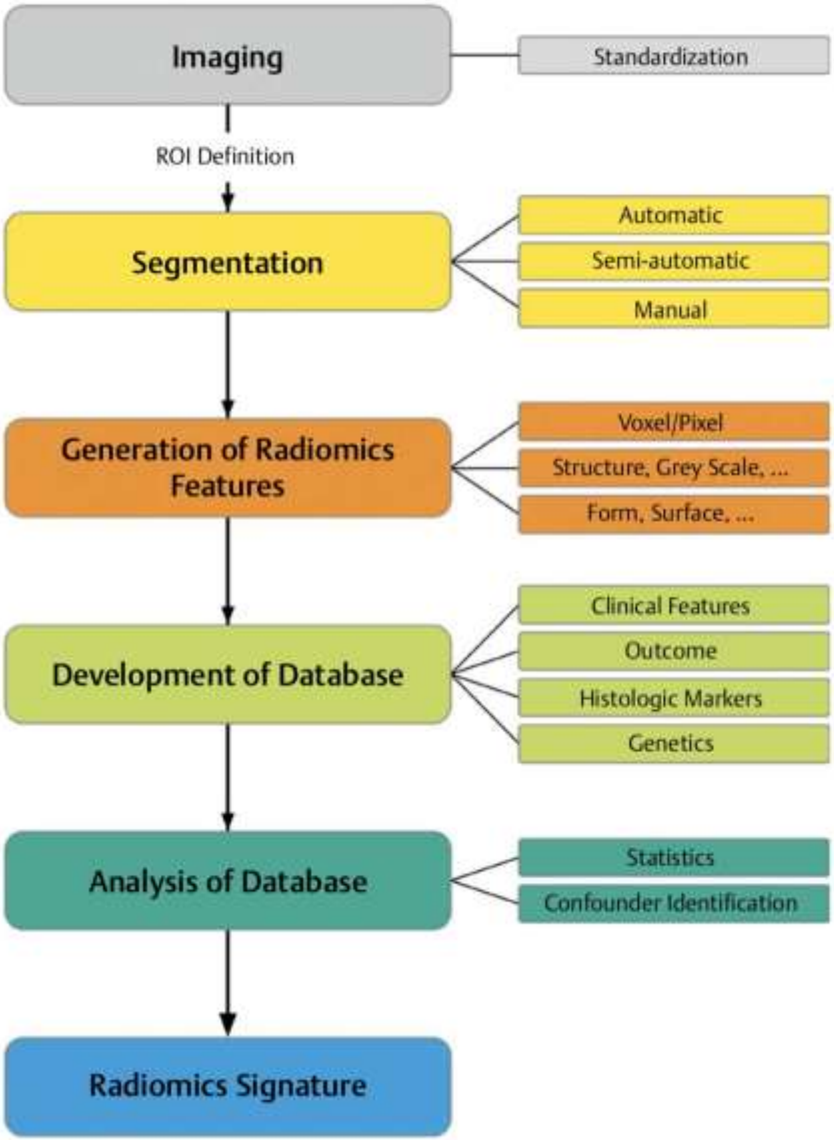
E. J. Limkin et al. Ann Oncol. 2017 Jun

Radiomics

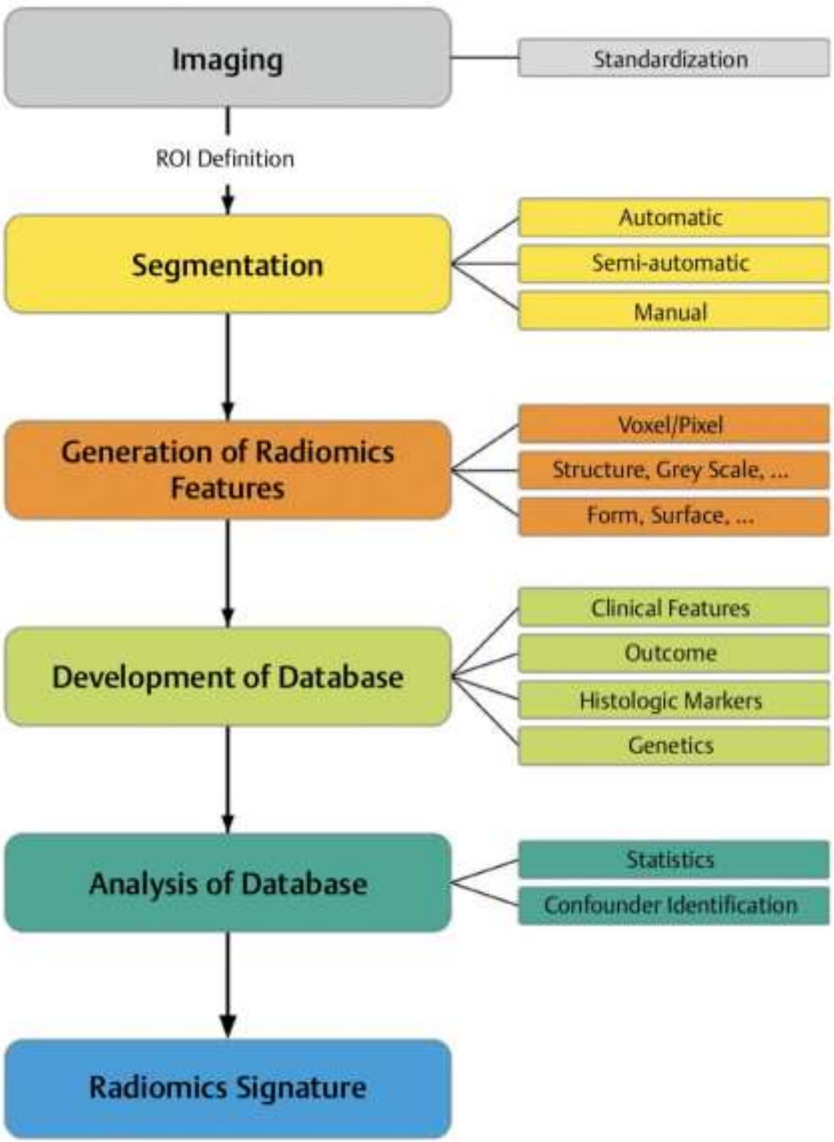
Radiomics: Images Are More than Pictures, They Are Data[1]

- ✓ *medical physicist*
- ✓ *biomedical engineer*

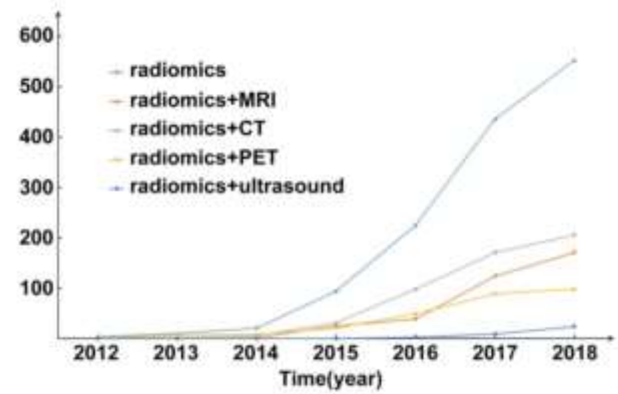
Radiomics – Work Flow



Radiomics – Work Flow



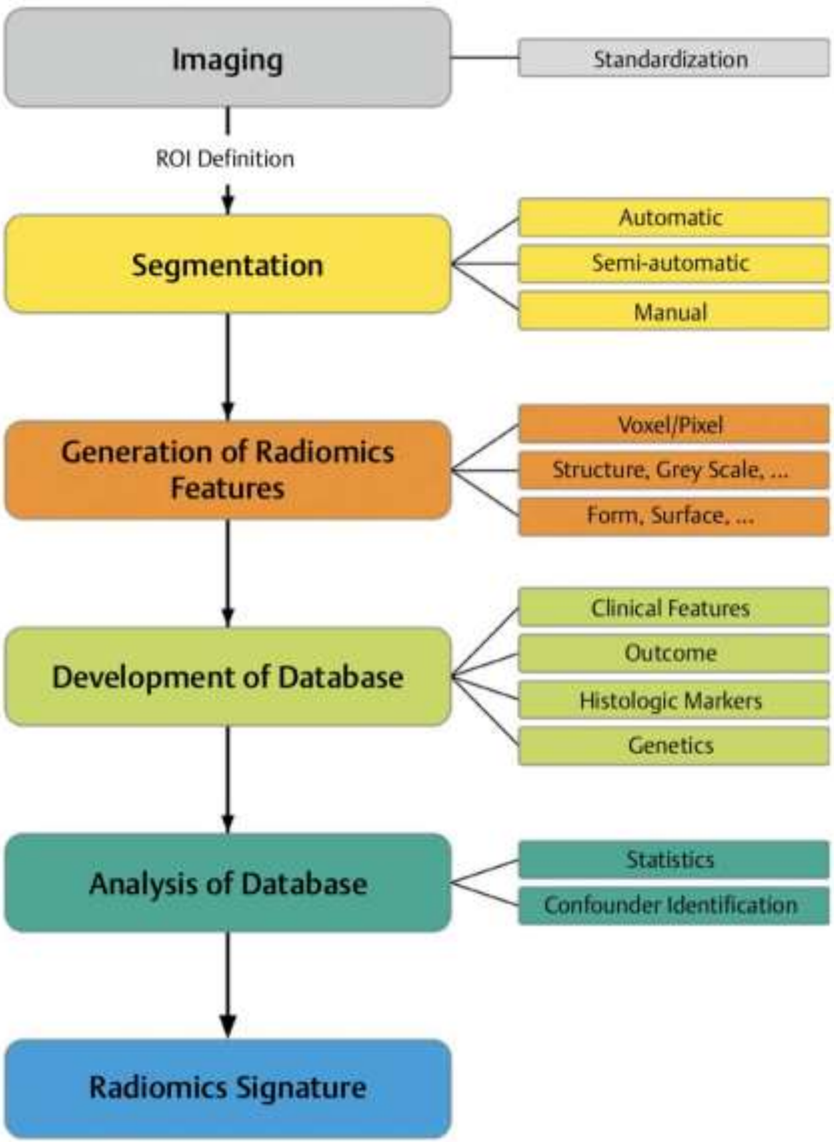
1. *RX*
2. *US*
3. *MX*
4. *CT*
5. *MR*
6. *PET-CT*




Theranostics

The Applications of Radiomics in Precision Diagnosis and Treatment of Oncology: Opportunities and Challenges

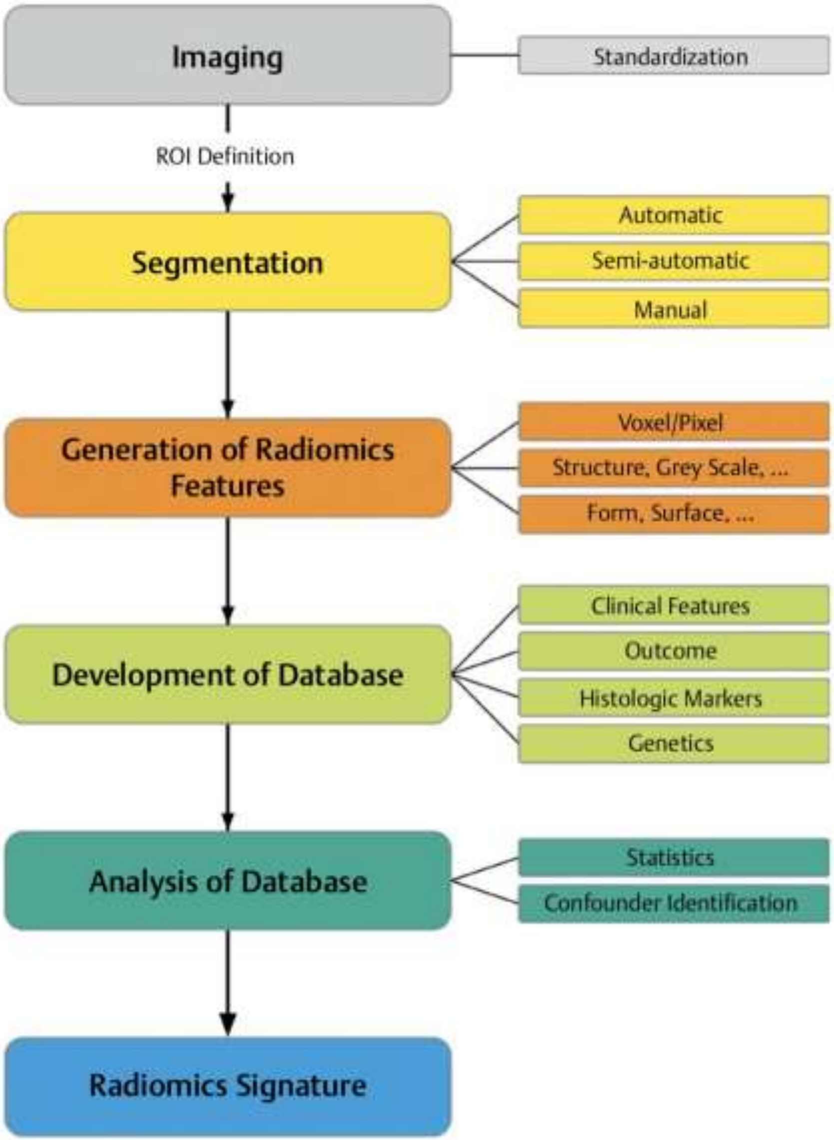
Radiomics – Work Flow

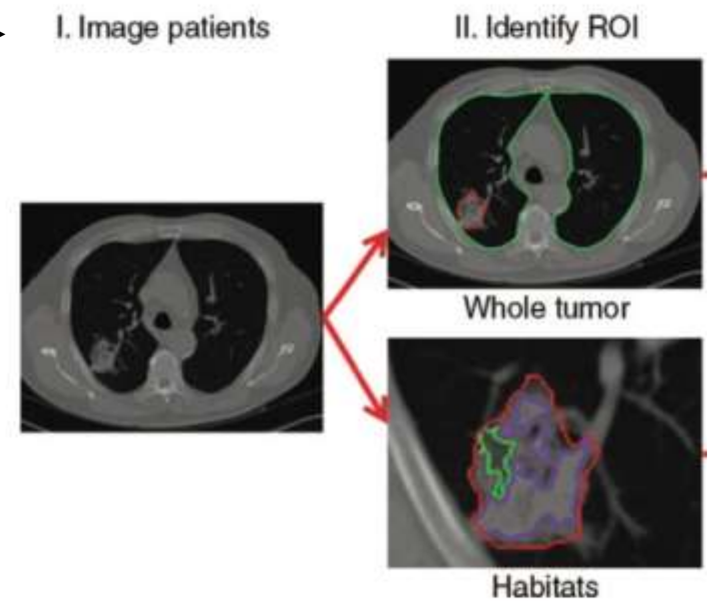


*traditionally, radiomics was developed for **extraction of features** from a **single modality** (e.g. **CT scans** on patients with **lung cancer**)*

*images used for radiomic analysis are collected from **different hospitals or data centers**; thus, these images are usually obtained using **different parameters and protocols and reconstructed** with different software.*
The differences may bring unexpected influences on the radiomic model

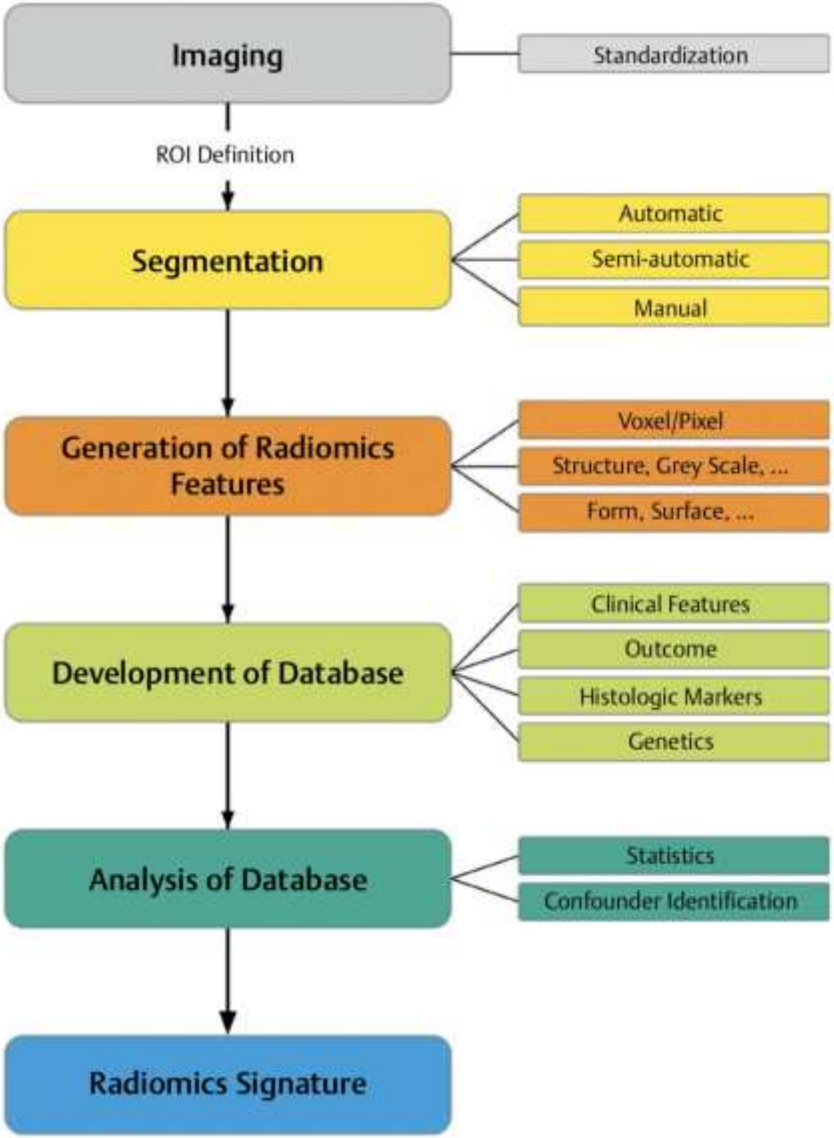
Radiomics – Work Flow





it is critical because the subsequent feature data are generated from the segmented volumes. It is challenging because many tumors have indistinct borders.

Radiomics – Work Flow



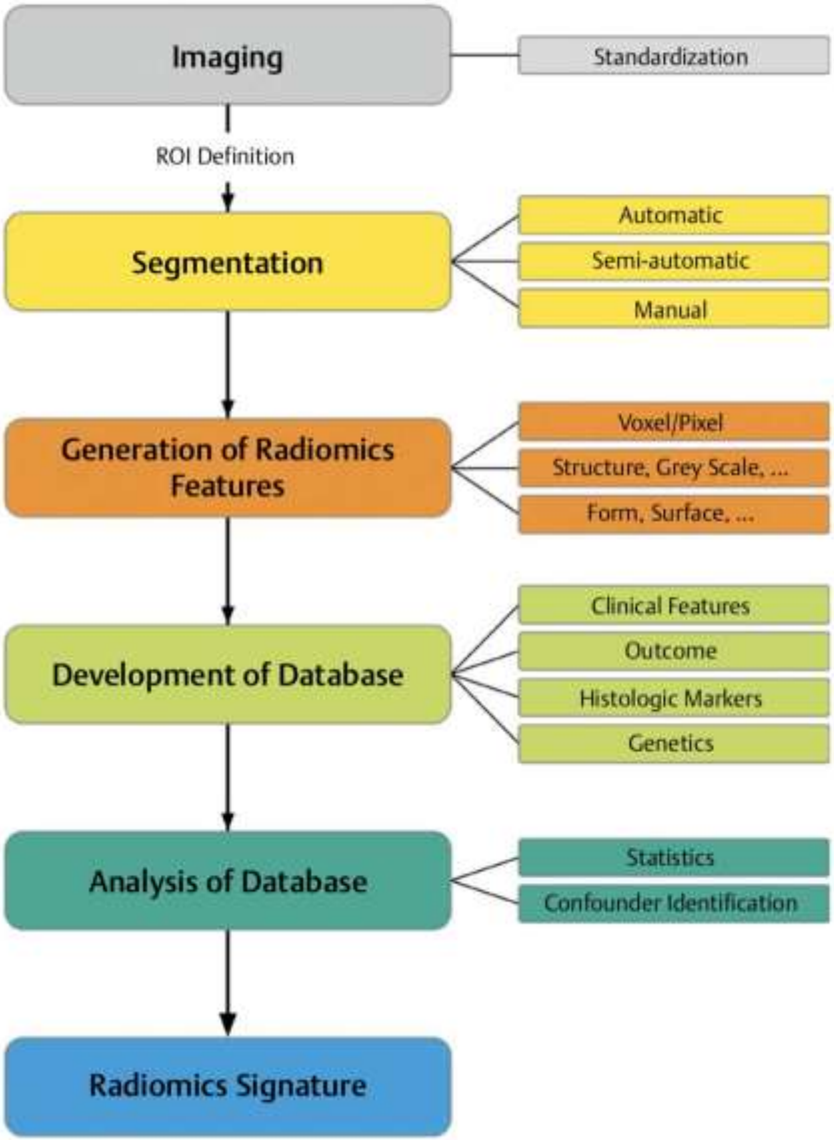
Extraction of Semantic features

- *dimension*
- *necrosis*
- *margin*
- *location*

Extraction of Non Semantic features

- ✓ *shape*
- ✓ *hystogram*
- ✓ *texture*

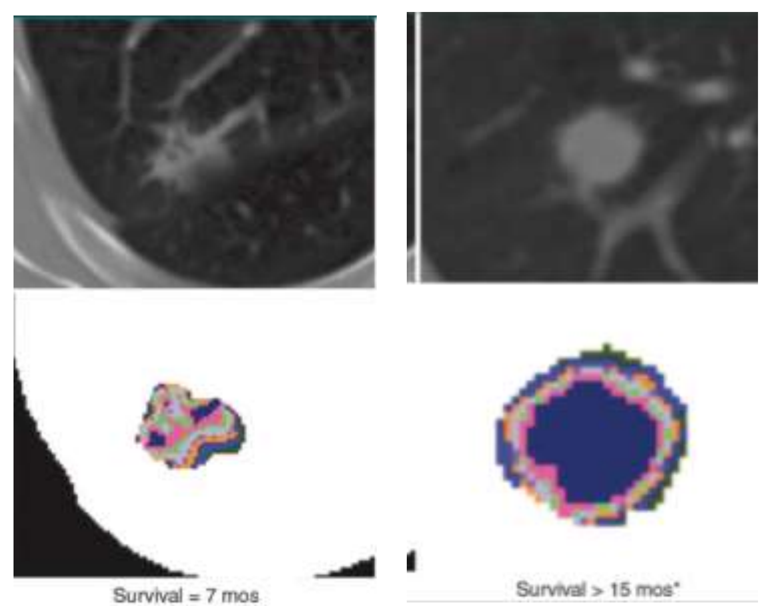
Radiomics – Work Flow



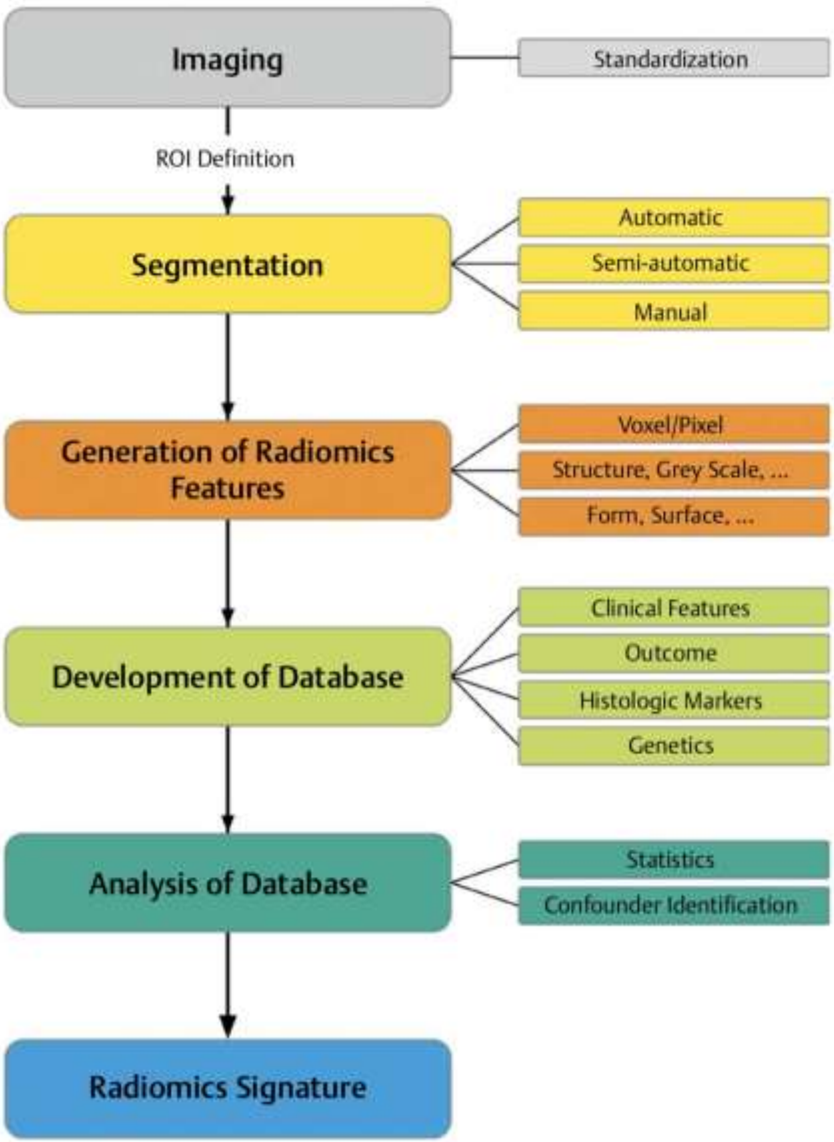
Extraction of
Non Semantic features

- *shape*

features describing the tumors, including volume, surface area, compactness

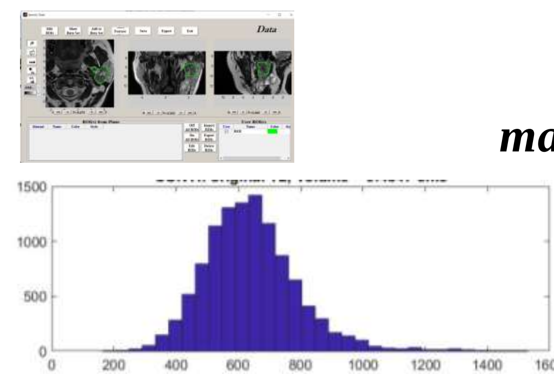


Radiomics – Work Flow

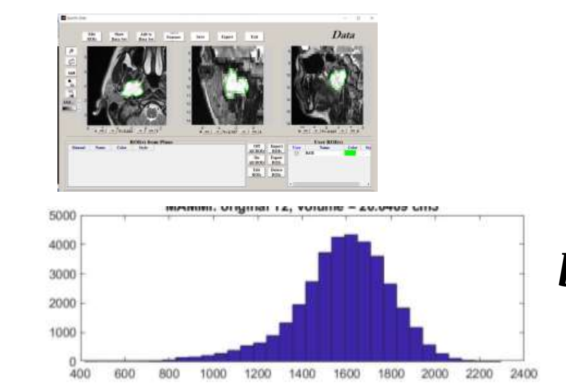


Extraction of
Non Semantic features

hystogram

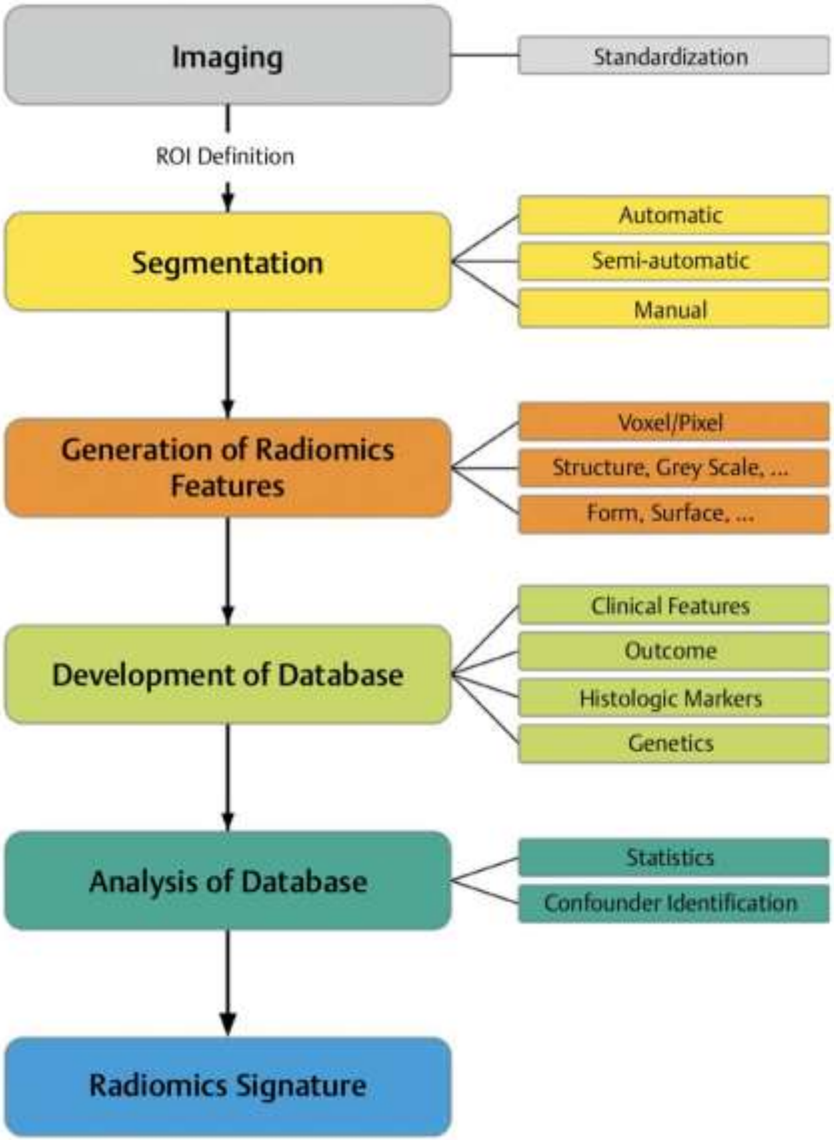


malignat



benign

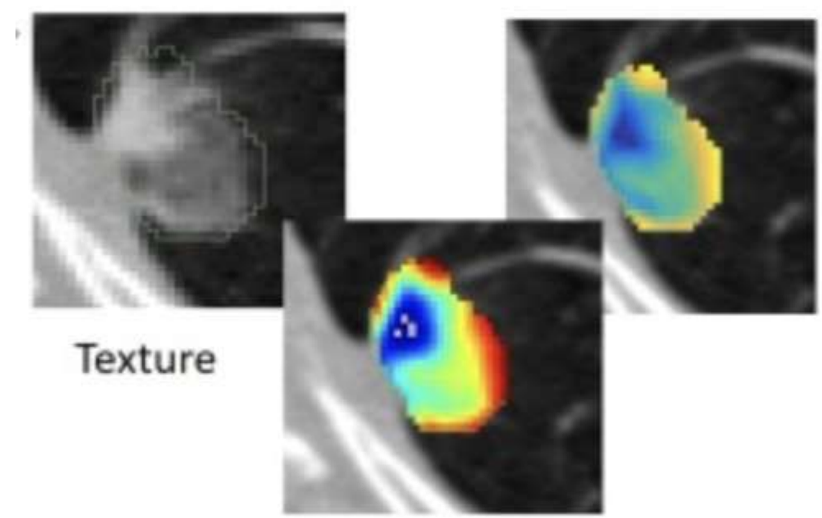
Radiomics – Work Flow



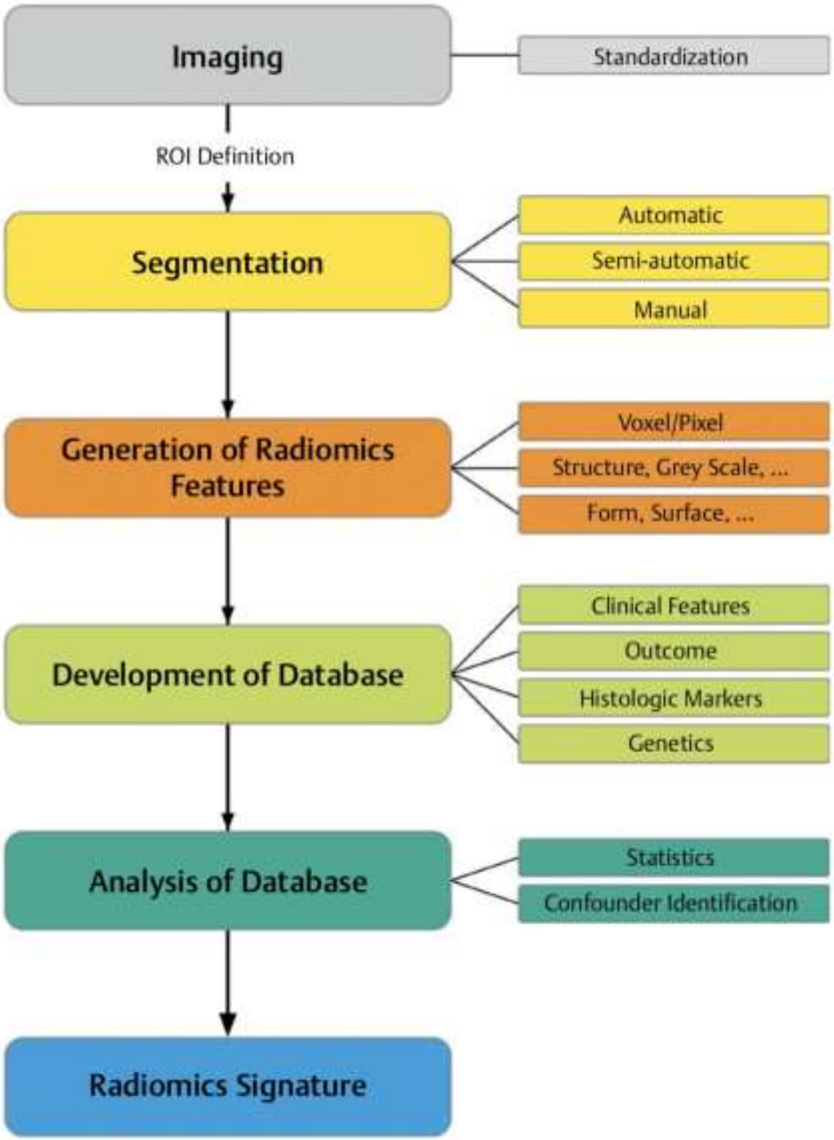
Extraction of
Non Semantic features

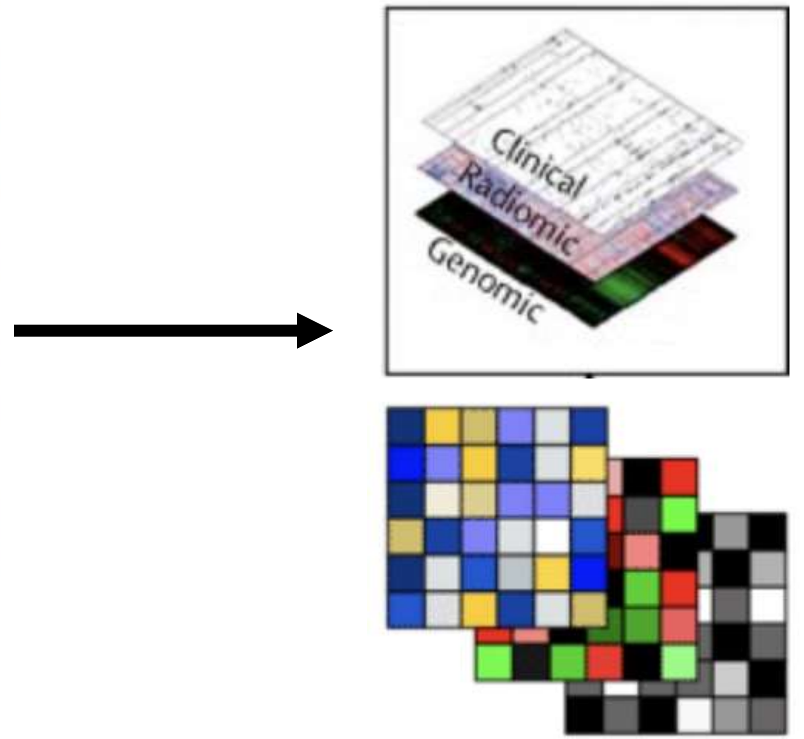
texture

heterogeneity

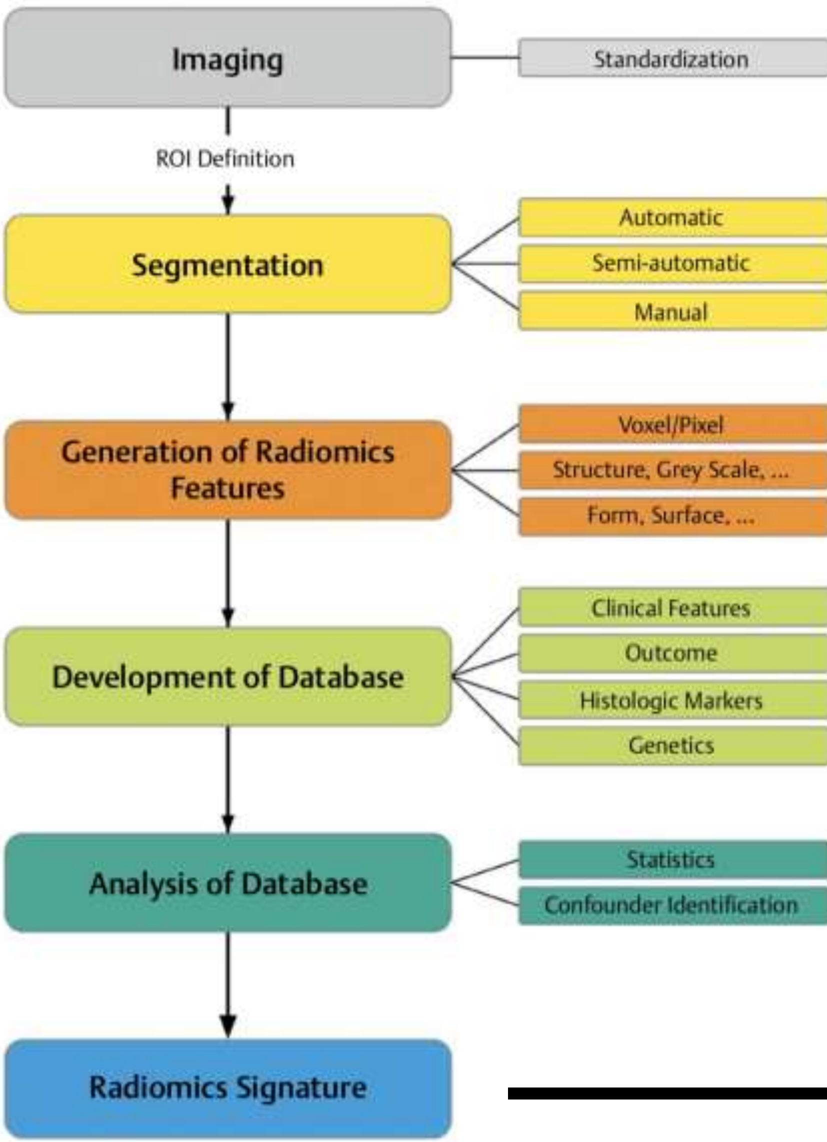


Radiomics – Work Flow

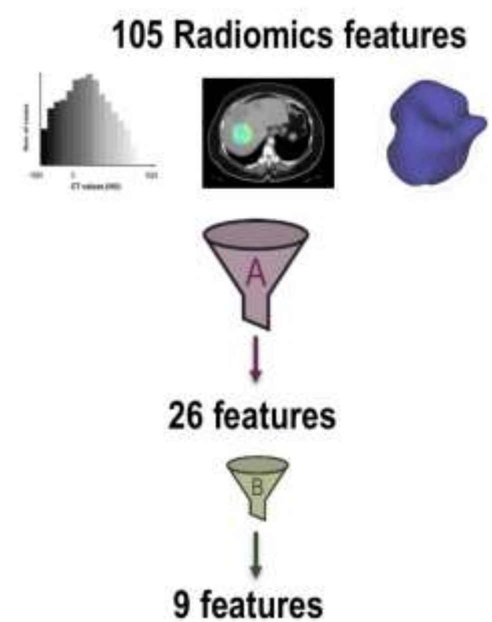




Radiomics – Work Flow



robust and informative features



Radiomic….some considerations

radiomics can be performed with as few as 100 patients, although larger data sets provide more power

- *radiomics….could potentially aid cance**r***

✓ *detection*
✓ *diagnosis*
✓ *assessment of prognosis*
✓ *prediction of response to treatment*
✓ *monitoring of disease status*

radiogenomics

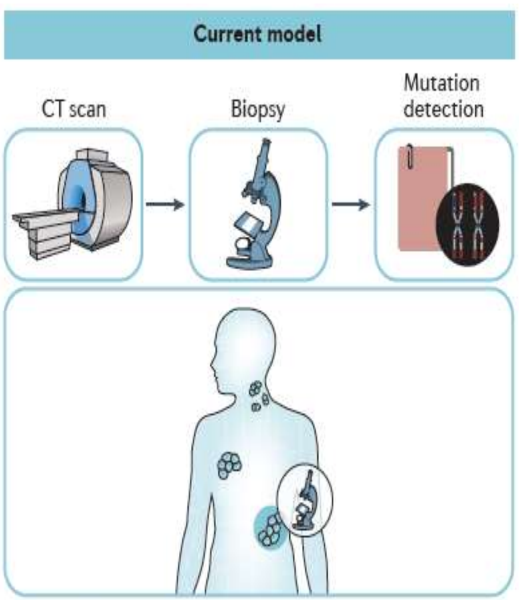
Radiomic

precision medicine

radiogenomics

two potential uses

…….a subset of the radiomic data can be used to suggest gene expression or mutation status that potentially warrants further testing. This is important because the radiomic data are derived from the entire tumor (or tumors) rather than from just a sample.



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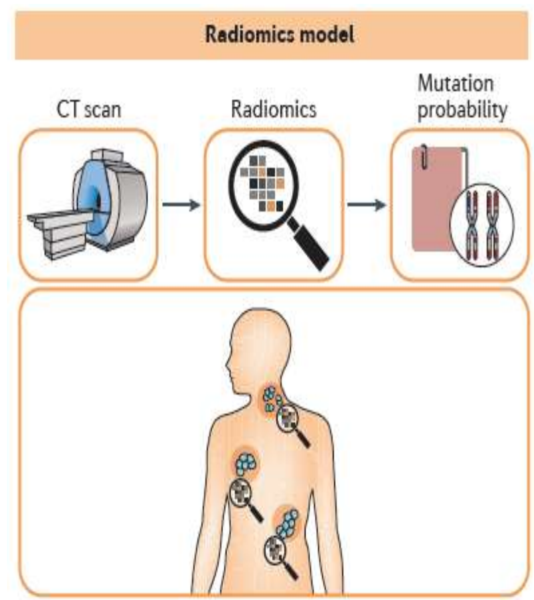
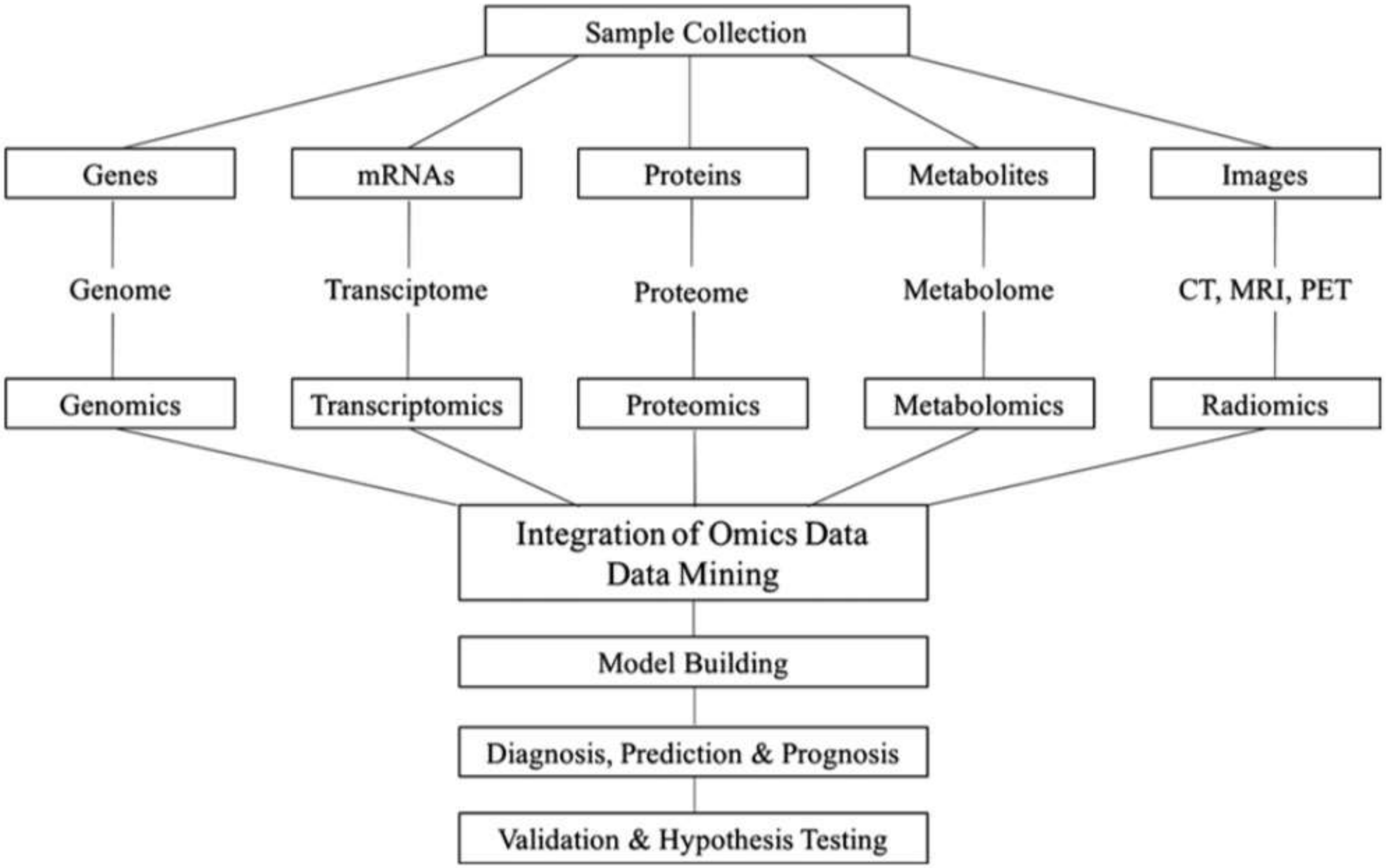


Work Flow



radiomics may reflect the global outlook of cancer

Radiomic *is designed to be used in decision support of* ***precision medicine***

most solid tumors are highly heterogeneous and that they continue to evolve over time; is the major cause of treatment failure and emergence of therapy resistance

precision medicine requires not only in vitro biomarkers and companion diagnostics but also spatially and temporally resolved in vivo biomarkers of tumor biology

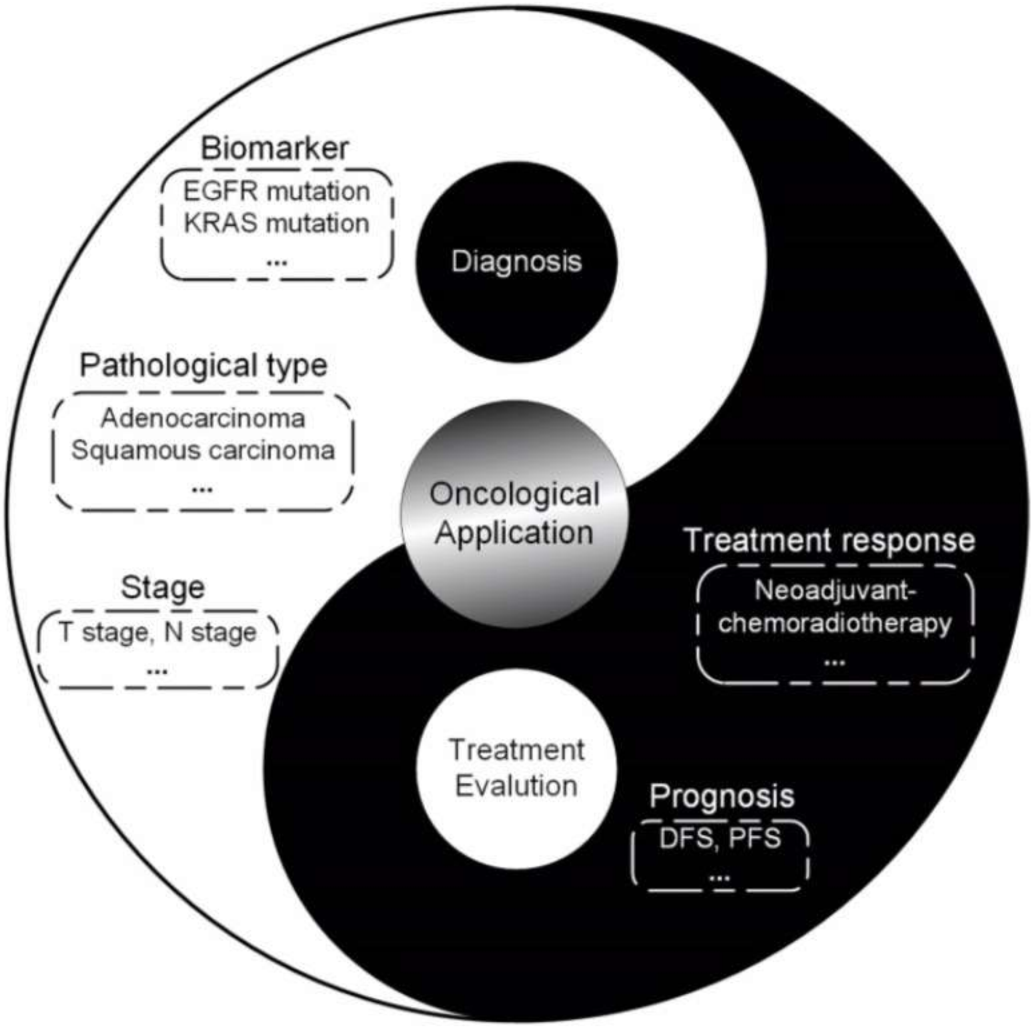
a central hypothesis driving radiomics research is that radiomics has the potential to enable quantitative measurement of intra- and intertumoral heterogeneity

radiomics is capable of capturing the entire tumor volume and allows longitudinal monitoring

Radiomic *is designed to be used in decision support of* ***precision medicine***

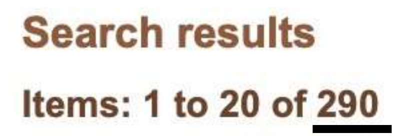
- ✓ ***use standard of care images*** that are routinely acquired in clinical practice, it presents a cost-effective and highly feasible addition for clinical decision support;
- ✓ ***non-invasively*** characterize the overall tumor accounting for heterogeneity;
- ✓ ***interrogates the entire tumor*** allows the expression of microscopic genomic and proteomics patterns in terms of macroscopic image-based features;
- ✓ ***produce*** prognostic and/or predictive biomarker value derived from routine, standard of care imaging data as-is;
- ✓ ***allow*** for a fast, low-cost, and repeatable means for longitudinal monitoring.

Radiomic….in Oncology



Radiomic….in Oncology

Lung cancer



Breast cancer

Radiomic….in Oncology

Lung cancer

Search results

Items: 1 to 20 of 30

Breast cancer

Search results

Items: 1 to 20 of 41

Radiomic….in Oncology

Lung cancer

differentiated aggressive lung carcinomas from non-aggressive ones based on CT scans

440 radiomic features in non-small cell lung and head and neck cancer. ***survival,*** the ***histology,*** and the ***tumor stage***

33 markers may ***predict metastatic spread***, and another signature encompassing 12 features the survival

differentiate distinct phenotypes (carcinoma in situ versus minimally invasive carcinoma versus invasive carcinoma)

radiomic signature (heterogeneity-based) in 353 patients ***could predict the EGFR*** (epidermal growth factor receptor) status; intended to ***differentiate KRAS-positive from KRAS-negative tumors***

Radiomic….in Oncology

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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Lung cancer

Identification of a Radio-Immune Signature with High Prognostic Value in Surgically Resected NSCLC

Date	29 September 2019
Event	ESMO 2019 Congress
Session	Poster Discussion session - Basic science
Presenter	Giulia Mazzaschi
Citation	Annals of Oncology (2019) 30 (suppl_5): v797-v815. 10.1093/annonc/mdz269
Authors	G. Mazzaschi[1], F. Quaini[2], G. Milanese[3], L. Gnetti[4], G. Bocchialini[2], L. Ampollini[2], R. Minari[5], M. Silva[3], N. Sverzellati[3], G. Roti[2], M. Tiseo[1] Author Affiliations

Background

The role of radiomics against clinical and histologic standard has been repeatedly demonstrated, although the integration of high-throughput imaging into a multidimensional prediction model is still in its early dawn. Thus, the aim of the present study was to determine whether CT-derived radiomic features (CT-RFs) might intercept the landscaped arrangement of the tumor immune microenvironment (TIME), offering a novel non-invasive assessment of prognostic factors in NSCLC.

Conclusions

Specific TIME profiles inscribe radiomic features resulting in a radio-immune signature with prognostic impact on NSCLC.

Deep Learning Radiomics distinguishes intrapulmonary Disease from Metastases in Immunotherapy-treated Melanoma Patients

Date	30 September 2019
Event	ESMO 2019 Congress
Session	Poster Display session 3
Topics	Melanoma Immunotherapy
Presenter	Thi Dan Linh Nguyen-Kim
Citation	Annals of Oncology (2019) 30 (suppl_5): v475-v532. 10.1093/annonc/mdz253
Authors	T.D.L. Nguyen-Kim[1], S. Trebeschi[2], J.E.E. Pouw[2], G. Milanese[3], L. Topff[2], Z. Bodalai[2], J. Mangana[4], T. Frauenfelder[1], J.B.A.G. Haanen[3], C.U. Blank[5], H.J.W.L. Aerts[6], R. Beets-Tan[2], R. Dummer[4] Author Affiliations

Conclusions

Deep learning can help to discriminate between intrapulmonary granulomatous disease, indeterminate calcified granulomas and intrapulmonary lymph nodes in anti-PD-1 treated melanoma patients. Further model development is needed to overcome the imbalanced "real clinical scenario" data to classify granulomatous disease in melanoma patients treated with anti-PD-1 immune checkpoint inhibitor blockade for implementation in the clinical workflow.

Radiomic….in Oncology

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Lung cancer

Radiomic Signatures for Identification of Tumors Sensitive to Nivolumab or Docetaxel in Squamous Non-Small Cell Lung Cancer (sqNSCLC)

Date	30 September 2019
Event	ESMO 2019 Congress
Session	Poster Display session 3
Topics	**Non-Small Cell Lung Cancer** **Translational Research**
Presenter	Laurent Dercle
Citation	Annals of Oncology (2019) 30 (suppl_5): v760-v796. 10.1093/annonc/mdz268
Authors	L. Dercle[1], M. Fronheiser[2], L. Lu[1], S. Du[2], W. Hayes[2], D.K. Leung[2], A. Roy[3], L.H. Schwartz[1], B. Zhao[1] **Author Affiliations**

» Conclusions

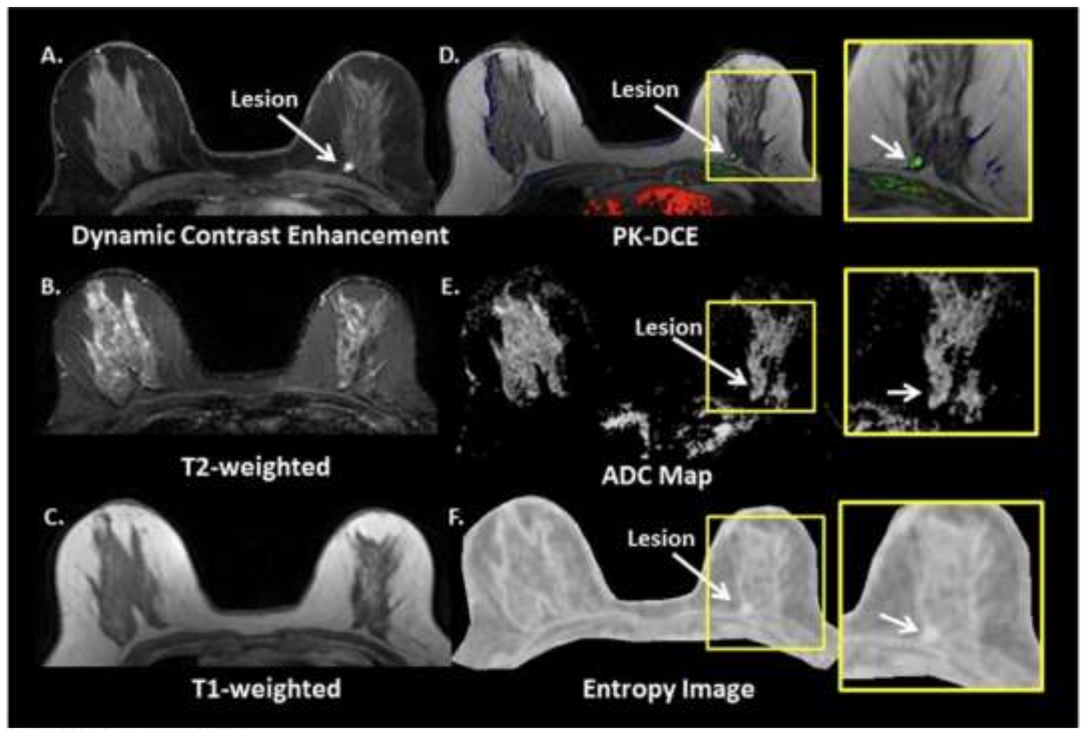
AI-based CT imaging detected early changes in radiomic features from baseline to first on-treatment tumor assessment—decrease in tumor volume, tumor heterogeneity, and tumor infiltrativeness along boundaries—that were associated with sensitivity to treatment in pts with sqNSCLC, offering an approach that could guide clinical decision-making to continue or modify systemic therapies.

Radiomic….in Oncology

Breast cancer

structural analysis of mammograms has also been successfully implemented in ultrasound diagnostics for ***differentiation of breast cancer***

magnetic resonance imaging



Published in npj Breast Cancer 2017

Integrated radiomic framework for breast cancer and tumor biology using advanced machine learning and multiparametric MRI

Vishwa S. Parekh, M. A. Jacobs

Radiomic….in Oncology

Breast cancer

structural analysis of mammograms has also been successfully implemented in ultrasound diagnostics for ***differentiation of breast cancer***

magnetic resonance imaging

differentiate breast cancer from benign lesions with a sensitivity of 85 % and a specificity of 89 %. By means of 3 classic machine-learning and 5 features

breast MR imaging radiogenomics can more fully ***assess the correlations between imaging features and breast cancer molecular subtypes*** of luminal A, luminal B, HER2, and TN cancer

differences between chemotherapy responders and failures based on 8 and 2 (entropy and uniformity) MRI-based structural parameters,

Radiomic….in Oncology

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Breast cancer

Prediction of benign and malignant breast masses using digital mammograms texture features

Date	30 September 2019
Event	ESMO 2019 Congress
Session	Poster Display session 3
Topics	**Breast Cancer** **Translational Research**
Presenter	Cui Yanhua
Citation	Annals of Oncology (2019) 30 (suppl_5): v574-v584. 10.1093/annonc/mdz257
Authors	C. Yanhua[1], Y. Li[2], J. zhu[3], J. dong[4] **Author Affiliations**

» Conclusions

Radiomics texture features from digital mammograms may be used for benign and malignant prediction. This method offer better accuracy and sensitivity. It is expected to provide an auxiliary diagnosis for the imaging doctors.

Radiomic….in Oncology

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Artificial intelligence combining radiomics and clinical data for predicting response to immunotherapy

Date	28 September 2019
Event	ESMO 2019 Congress
Session	Proffered Paper session: Artificial intelligence and machine learning as tools for practice in oncology
Topics	**Imaging** **Personalised/Precision Medicine** **Immunotherapy** **Basic Principles in the Management and Treatment (of cancer)** **Therapy**
Presenter	Marta Ligero
Citation	Annals of Oncology (2019) 30 (suppl_5): v475-v532. 10.1093/annonc/mdz253
Authors	M. Ligero[1], A. Garcia-Ruiz[1], C. Viaplana[2], M.V. Raciti[1], I. Matos[3], J. Martín Liberal[3], C. Hierro[4], M. Gonzalez[5], R. Morales Barrera[5], C. Suárez[5], E. Elez[5], I. Brana[5], E. Muñoz-Couselo[5], A. Oaknin[3], E. Felip[4], J. Tabernero[5], J. Carles[5], R. Dienstmann[2], E. Garralda[5], R. Perez Lopez[1] **Author Affiliations**

Conclusions

CT-radiomics signature at baseline predicts the response to immune checkpoint inhibitors. Integrating radiomics and clinical data improved the response prediction capacity.

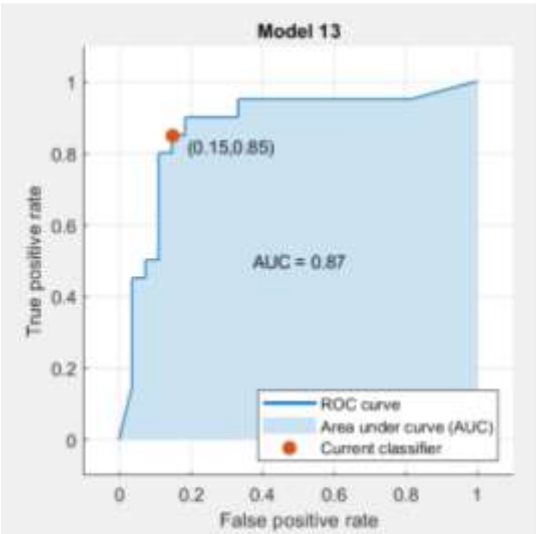
Radiomic….in Oncology

our experience

- ✓ *characterization*
- ✓ *prediction to response*

Radiomic….in Head and Neck

our experience



salivary gland lesions

1 benign
2 malignant

Model skewness ADC, mean T2,margin, contrast medium	Value	95% CI
Accuracy	**85,11**	**71.69% to 93.80%**
Sensitivity(%)	**88,5**	**69.85% to 97.55%**
Specificity(%)	**81,0**	**58.09% to 94.55%**
PPV(%)	**85,2**	**70.19% to 93.35%**
NPV(%)	**85,0**	**65.71% to 94.37%**

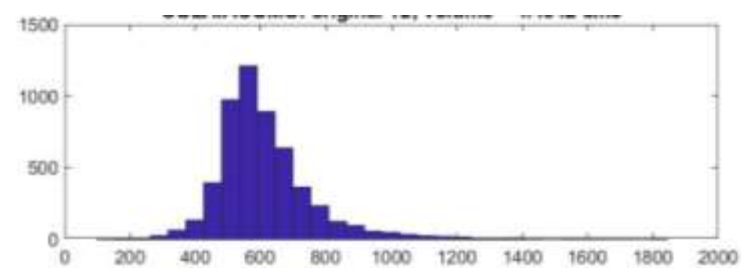
features

- *skewness ADC*
- *mean T2*
- *margin*
- *contrast medium*

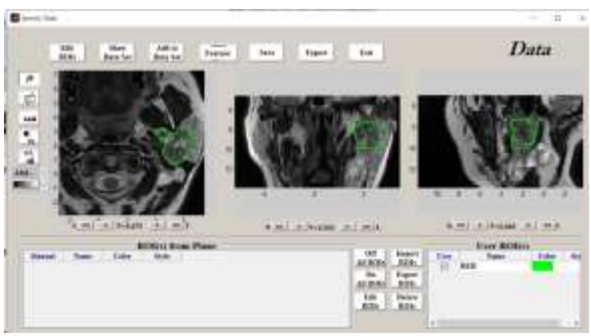
Radiomic….in Head and Neck

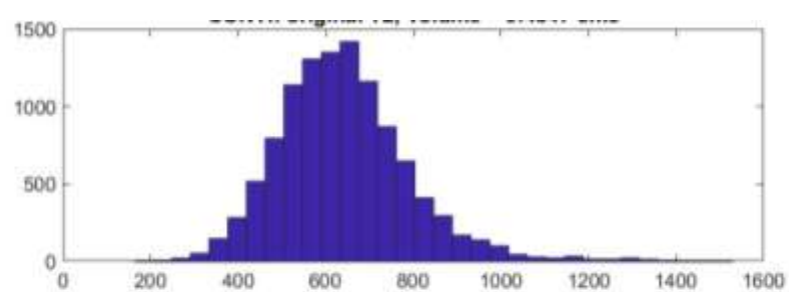
our experience

mean T2

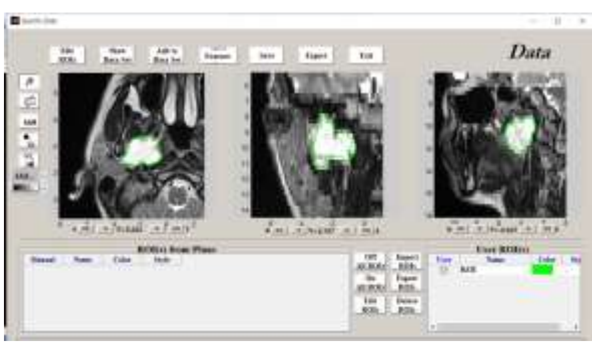


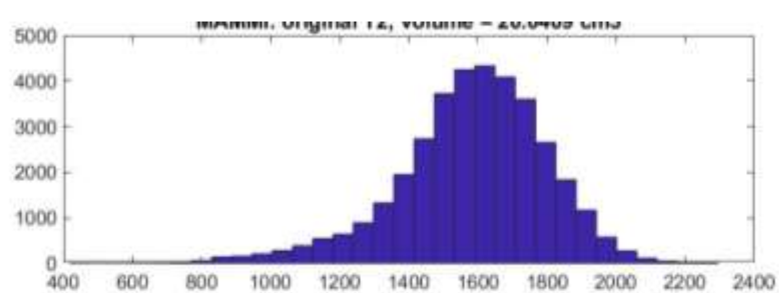
Warthin





Malignant





Pleomorhic Adenoma

Radiomic….in Head and Neck

our experience

European Journal of Radiology 119 (2019) 108640

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Research article

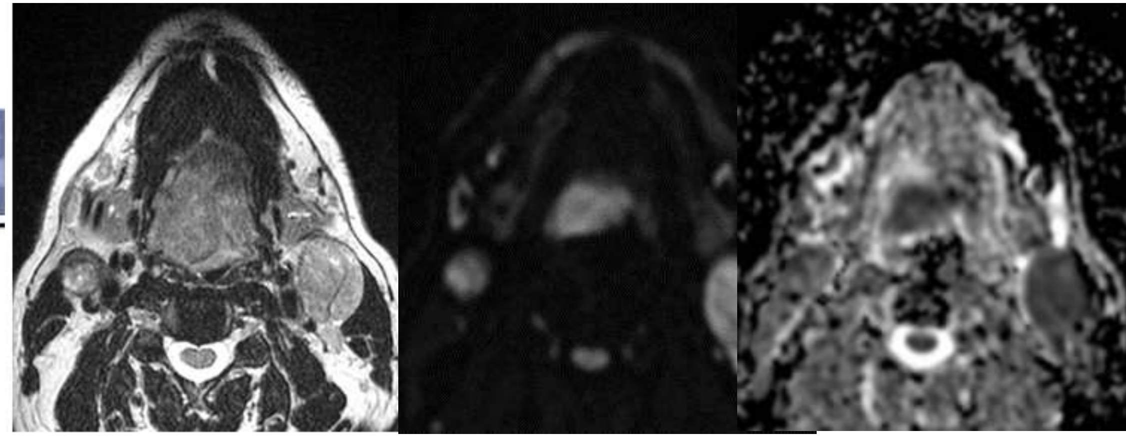
Intravoxel incoherent motion diffusion-weighted imaging for oropharyngeal squamous cell carcinoma: Correlation with human papillomavirus Status

Antonello Vidiri, Simona Marzi, Emma Gangemi, Maria Benevolo, Francesca Rollo, Alessia Farneti, Laura Marucci, Filomena Spasiano, Francesca Sperati, Francesca Di Giuliano, Raul Pellini, Giuseppe Sanguineti

Patient and tumor characteristics sorted by human papillomavirus (HPV) status.

Patient and tumor characteristics		HPV-negative	HPV-positive	Chi2
		(n = 19)	(n = 54)	p
		n(%)	n(%)	
Gender	*Male*	18 (30.5)	41 (69.5)	0.096
	Female	1 (7.1)	13 (92.9)	
Age (mean ± SD)		65.4 ± 9.1	61.7 ± 9.5	0.140
Tumour site	*Tonsil*	8 (20.0)	32 (80.0)	0.322
	Base of the tongue	11 (34.4)	21 (65.6)	
	Both	0 (0.0)	1 (100.0)	
T-stage	*T1-2*	7 (24.1)	22 (75.9)	0.765
	T3-4	12 (27.3)	32 (72.7)	
N-stage	*N0*	3 (60.0)	2 (40.0)	**<0.001**
	N1	1 (3.0)	32 (97.0)	
	N2-3	15 (42.9)	20 (57.1)	
Smoking status	*0-5pack/yr*	3 (10.3)	26 (89.7)	**0.003**
	6-24pack/yr	1 (9.1)	10 (90.9)	
	>24pack/yr	15 (45.5)	18 (54.5)	
Alcohol intake	*No*	6 (13.0)	40 (87.0)	**<0.001**
	Moderate	3 (21.4)	11 (78.6)	
	Heavy	10 (76.9)	3 (23.1)	
Nodal Morphology	*Solid*	9 (23.7)	29 (76.3)	0.996
	Cystic	1 (25)	3 (75)	
	Necrotic	6 (23.1)	20 (76.9)	

Statistically significant p-values are bold.

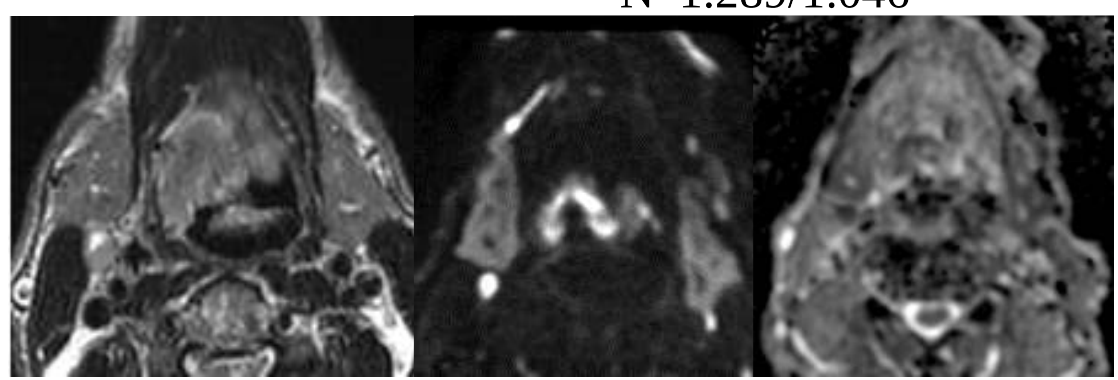


ADC/D_t T 1.377/0.991 ×10-3 mm2/s
N 0.953/0.738 × 10-3 mm2/s

lower ADC HPV+

higher ADC HPV-

ADC/D_t T 1.598/1.265 ×10-3 mm2/s
N 1.289/1.046 × 10-3 mm2/s



Radiomic….in Head and Neck

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European Journal of Radiology 119 (2019) 108640

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Research article

Intravoxel incoherent motion diffusion-weighted imaging for oropharyngeal squamous cell carcinoma: Correlation with human papillomavirus Status

Antonello Vidiri[a], Simona Marzi[b,*], Emma Gangemi[a], Maria Benevolo[c], Francesca Rollo[c], Alessia Farneti[d], Laura Marucci[d], Filomena Spasiano[a], Francesca Sperati[e], Francesca Di Giuliano[a,f], Raul Pellini[g], Giuseppe Sanguineti[d]

Patient and tumor characteristics sorted by human papillomavirus (HPV) status.

Patient and tumor characteristics		HPV-negative	HPV-positive	Chi2
		(n = 19)	(n = 54)	p
		n(%)	n(%)	
Gender	*Male*	18 (30.5)	41 (69.5)	0.096
	Female	1 (7.1)	13 (92.9)	
Age (mean ± SD)		65.4 ± 9.1	61.7 ± 9.5	0.140
Tumour site	*Tonsil*	8 (20.0)	32 (80.0)	0.322
	Base of the tongue	11 (34.4)	21 (65.6)	
	Both	0 (0.0)	1 (100.0)	
T-stage	*T1-2*	7 (24.1)	22 (75.9)	0.765
	T3-4	12 (27.3)	32 (72.7)	
N-stage	*N0*	3 (60.0)	2 (40.0)	**<0.001**
	N1	1 (3.0)	32 (97.0)	
	N2-3	15 (42.9)	20 (57.1)	
Smoking status	*0-5pack/yr*	3 (10.3)	26 (89.7)	**0.003**
	6-24pack/yr	1 (9.1)	10 (90.9)	
	>24pack/yr	15 (45.5)	18 (54.5)	
Alcohol intake	*No*	6 (13.0)	40 (87.0)	**<0.001**
	Moderate	3 (21.4)	11 (78.6)	
	Heavy	10 (76.9)	3 (23.1)	
Nodal Morphology	*Solid*	9 (23.7)	29 (76.3)	0.996
	Cystic	1 (25)	3 (75)	
	Necrotic	6 (23.1)	20 (76.9)	

Statistically significant p-values are bold.

the best predictive model for HPV positivity was obtained combining

- ✓ alcohol intake
- ✓ smoke habits
- ✓ D_t values of PTs

accuracy = 80.8%

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Physica Medica

journal homepage: http://www.physicamedica.com

Original paper

Characterization of cervical lymph-nodes using a multi-parametric and multi-modal approach for an early prediction of tumor response to chemo-radiotherapy

Elisa Scalco[a,*,1], Simona Marzi[b,1], Giuseppe Sanguineti[c], Antonello Vidiri[d], Giovanna Rizzo[a]

Patient characteristics.

Characteristic	No.
Patient number	30
Age (years)	
Median (range)	58 (28–82)
Sex (M/F)	27/3
Primary tumor site	
Oropharynx	12 (40.0%)
Nasopharynx	11 (36.7%)
Hypopharynx	5 (16.7%)
Larynx	1 (3.3%)
Unknown	1 (3.3%)
T stage	
T1	6 (20%)
T2	11 (36.7%)
T3	5 (16.7%)
T4	7 (23.3%)
T0	1 (3.3%)
N stage	
N1	6 (20%)
N2a	4 (13.3%)
N2b	6 (20%)
N2c	8 (26.6%)
N3	6 (20%)
LN volume (cm^3)	
Median (range)	4 (0.8–44)

the image-based analysis was performed on

- *the planning CT*
- *on T2w-MRI*
- *DW-MRI acquired before CRT (MRI 1) and at mid-treatment (MRI 2)*

Complete list of the estimated features.

Morphological features (T2w-MRI)		First-order statistical features (T2w-MRI, CT)		Second-order statistical features (T2w-MRI, CT)		Other features	
Volume	*V [mm^3]*	Mean intensity	μ	Energy	*GLCM_en*	Fractal dimension (T2w-MRI, CT)	*FD*
Eccentricity	*Ecc*	Variance	σ^2	Correlation	*GLCM_corr*		
Equivalent diameter	*Eq_diam [mm]*	Entropy	*ent*	Homogeneity	*GLCM_homo*	Apparent diffusion coefficient (DW-MRI)	*ADC [mm^2/s]*
		Skewness	*sk*	Entropy	*GLCM_ent*		
		Kurtosis	*kur*	Contrast	*GLCM_cont*		
				Dissimilarity	*GLCM_dis*		

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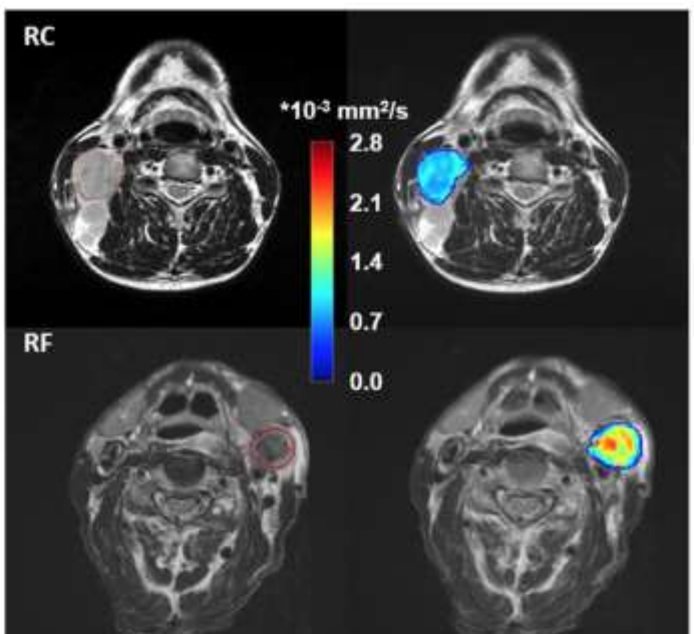


pre-treatment features showed higher predictive power than mid-CRT features, the ADC having the highest accuracy (80%); CT-based indices were found not predictive. When ADC was combined with Texture Analisys on T2, the classification performance increased ***(accuracy = 82.8%)***

clinical information

age – sex

site-subsite

T - N stage

therapeutic combination

hystogram analysis

mean

median

kurtosis

skewness

entropy

cellular information

Diffusion

ADC - D - f

D - K - Dk*

microcirculation information

Perfusion

nIAUGC - Ktrans

Ve – Kep - Vp

CT/MR morpholgycal information

dimension - necrosis

shape- margin

gray level on CT

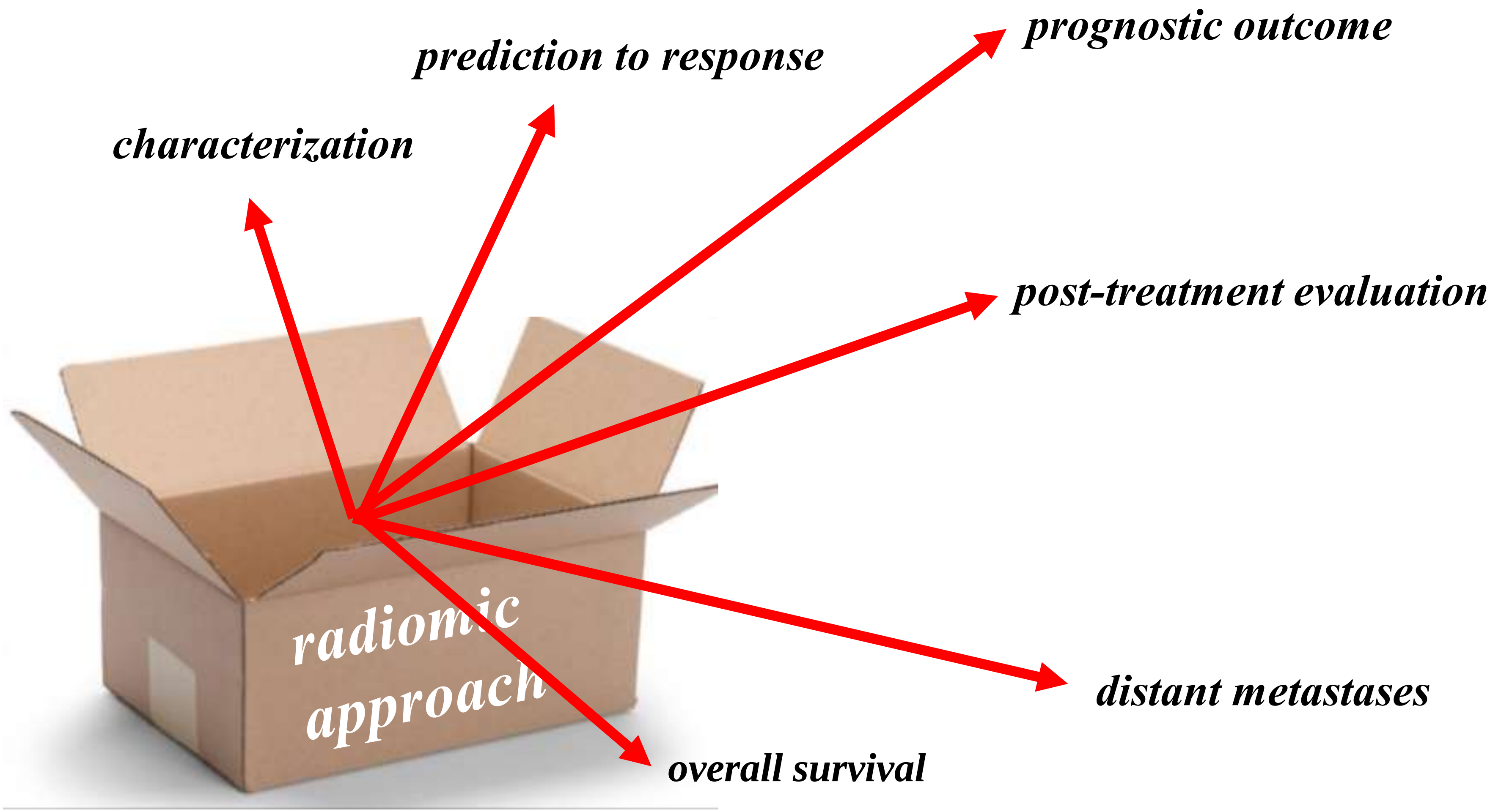
MR T2 signal intensity

contrast medium

metabolic information

PET-CT

SUV


prognostic outcome
prediction to response
characterization
post-treatment evaluation
radiomic approach
distant metastases
overall survival

Challenges

- ✓ Understanding (what do GLRLM, SRL….)
- ✓ Standardization ?
- ✓ Acquisition variability ?
- ✓ Representative populations ?
- ✓ Medical meaning/usefulness ?

…..still a long way to go
as any challenges

Radiomics

- ✓ ***Radio***
- ✓ ***Omics***

  genomics (DNA)
  transcriptomics (RNA)
  proteomics
  metabolomics