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ISTITUTO NAZIONALE TUMORI
REGINA ELENA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

Radiomics

Antonello Vidiri

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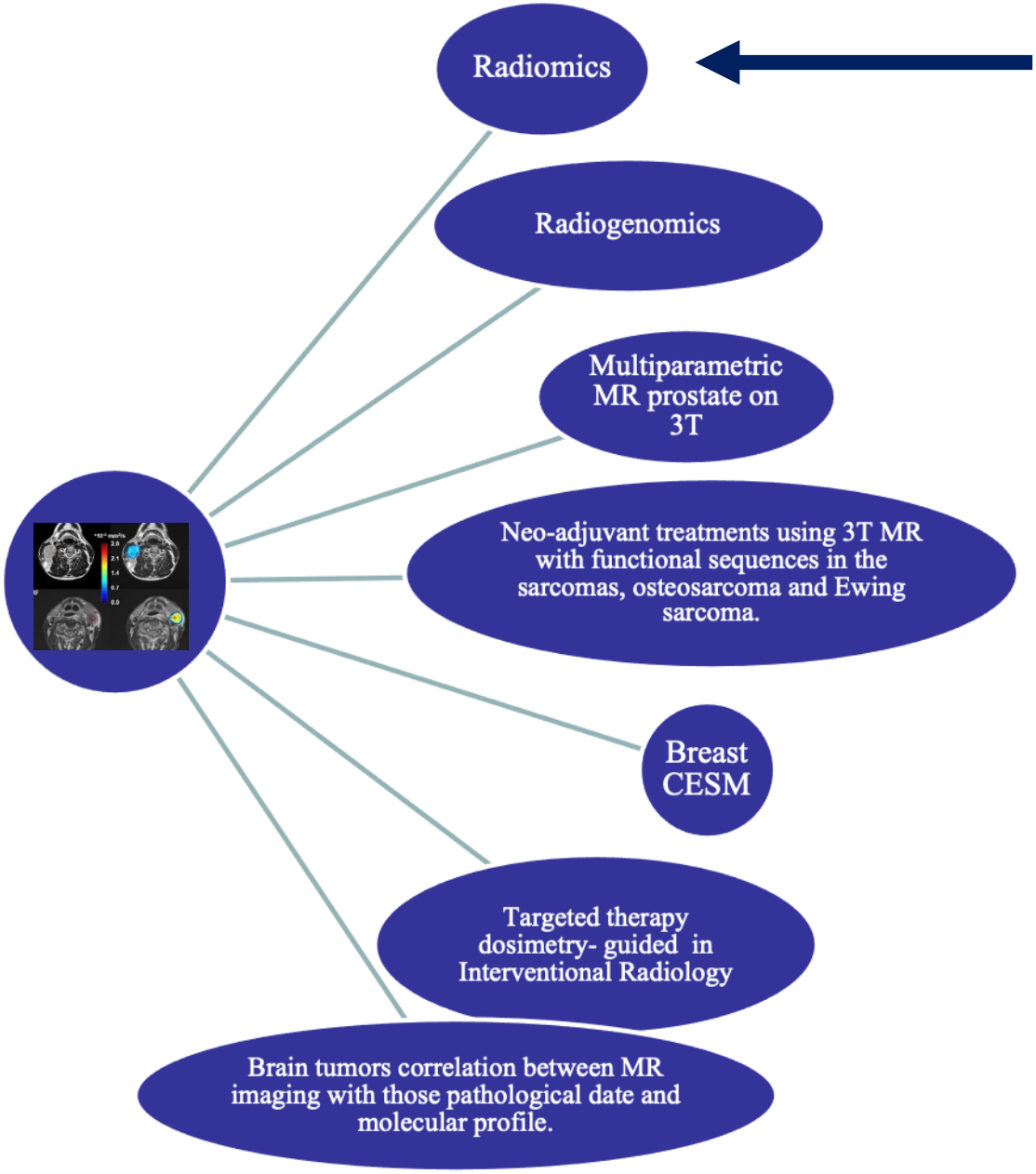
IRCSS Regina Elena National Cancer Institute

Specific topics of research of Radiology Unit



Aims

- ✓ *tissue characterization*
- ✓ *early diagnosis*
- ✓ *prediction of response to treatment*

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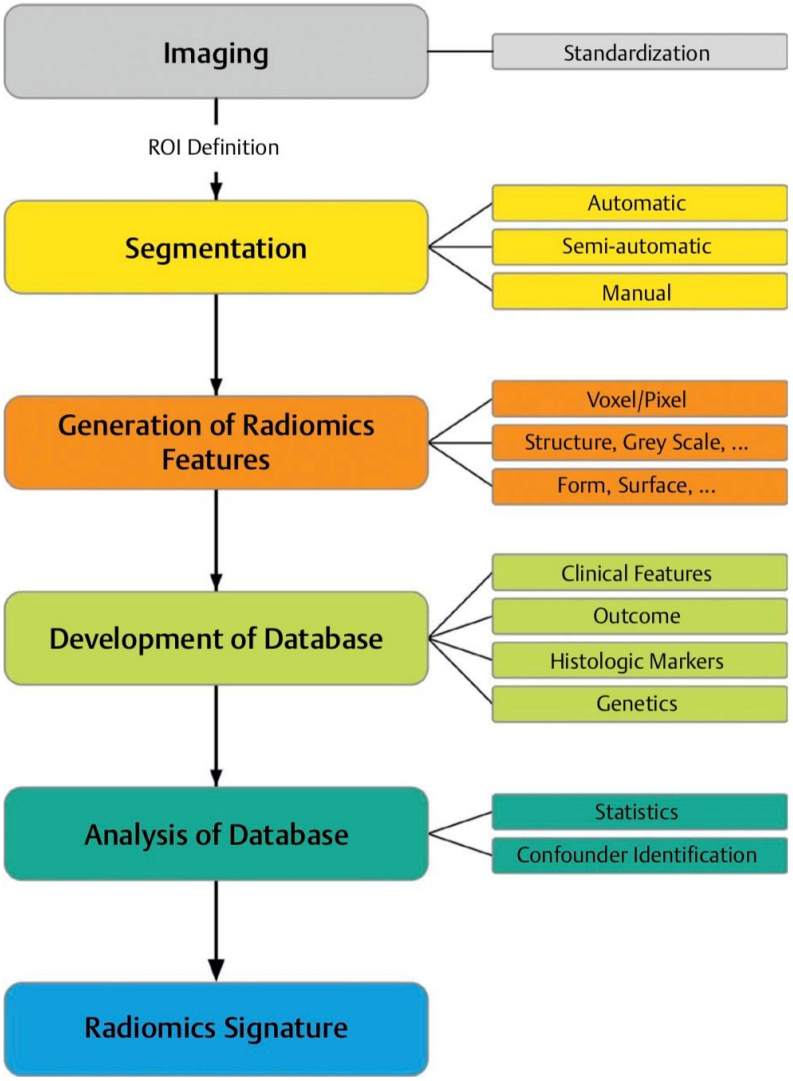
Radiomics: Images Are More than Pictures, They Are Data[1]

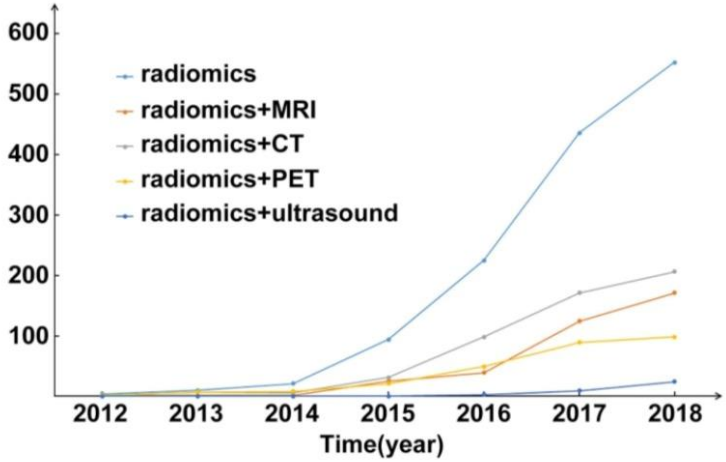
…the extraction of a high number of quantitative features from medical images on regions of interest (ROIs)

quantification of tumor phenotype

Radiomics – Work Flow



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



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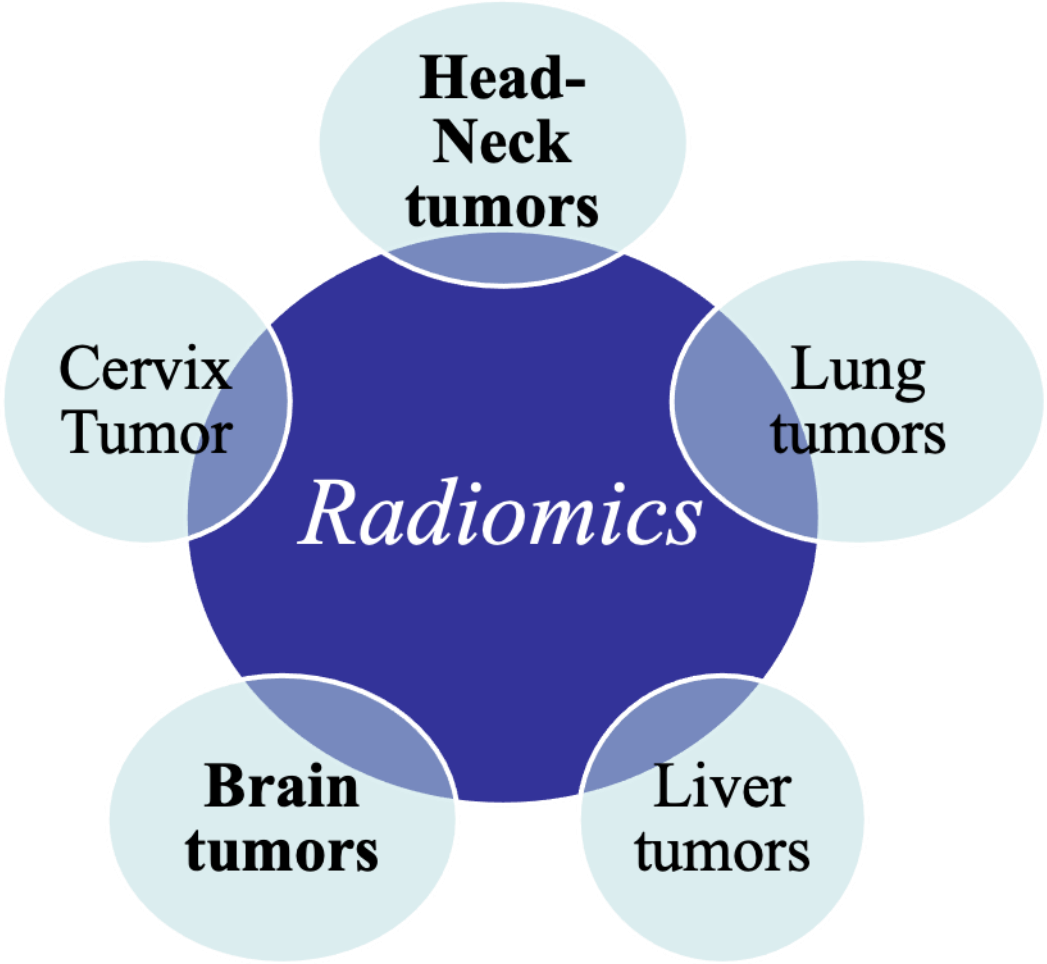
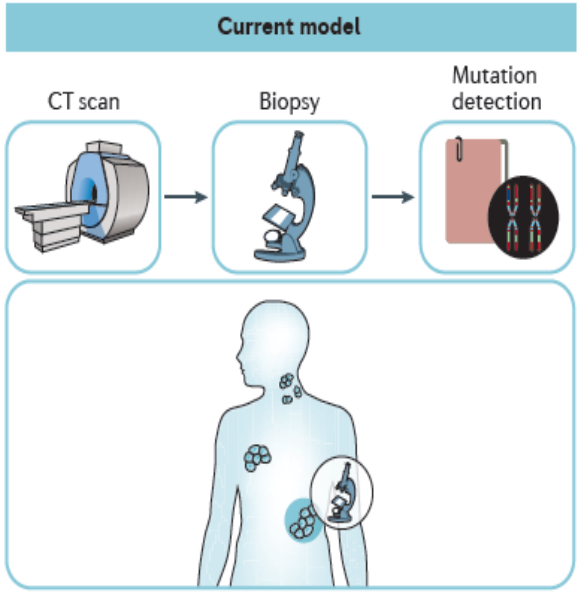
our topics of research



radiomics….could potentially aid in cancer:

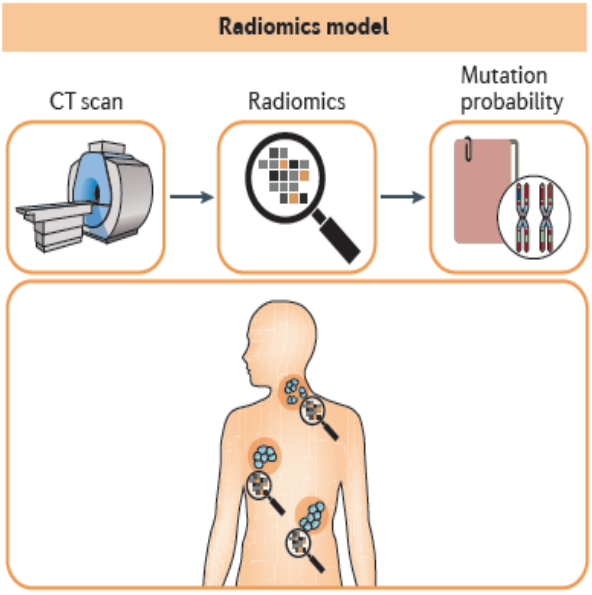
- ✓ *detection*
- ✓ *diagnosis*
- ✓ *assessment of prognosis*
- ✓ *prediction of response to treatment*
- ✓ *monitoring of disease status*

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



future....

....virtual biopsy



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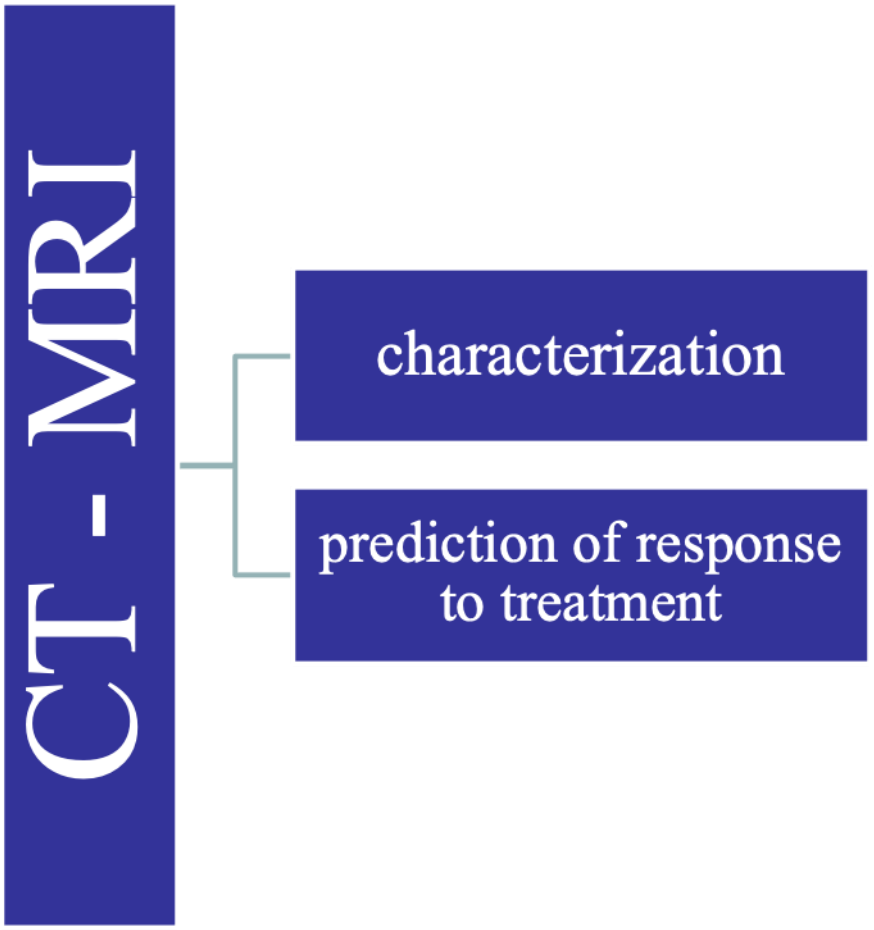


Extraction of
Semantic features

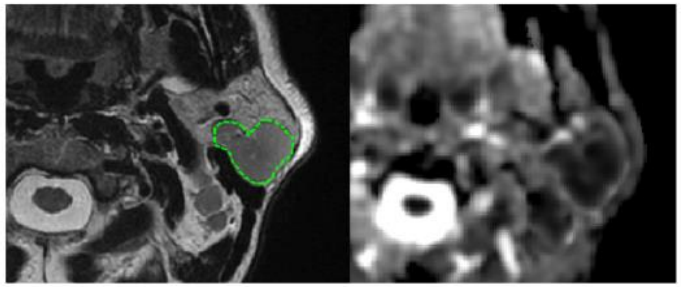
- *dimension*
- *necrosis*
- *margin*
- *location*

Extraction of
Non Semantic features

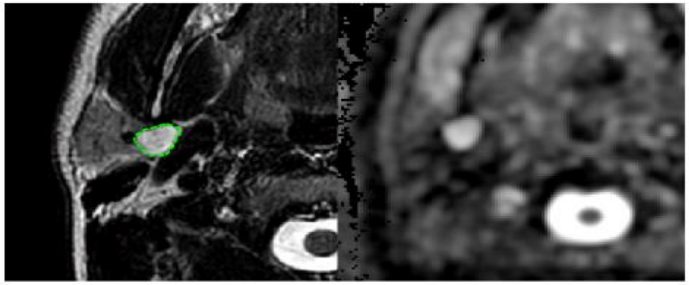
- ✓ *shape*
- ✓ *histogram*
- ✓ *texture*

Extraction of
Semantic features

- *margin*



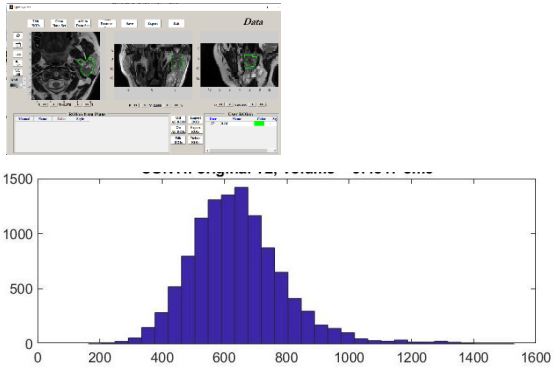
parotid lesions



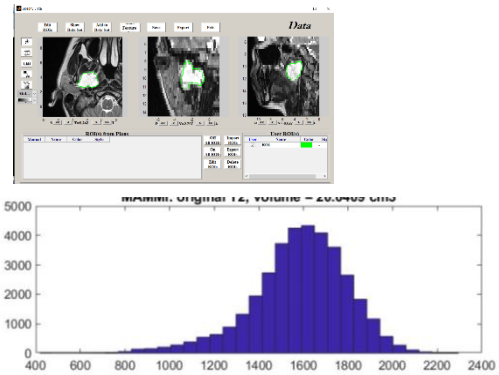
Extraction of
Non Semantic features

- *histogram*

malignant



benign



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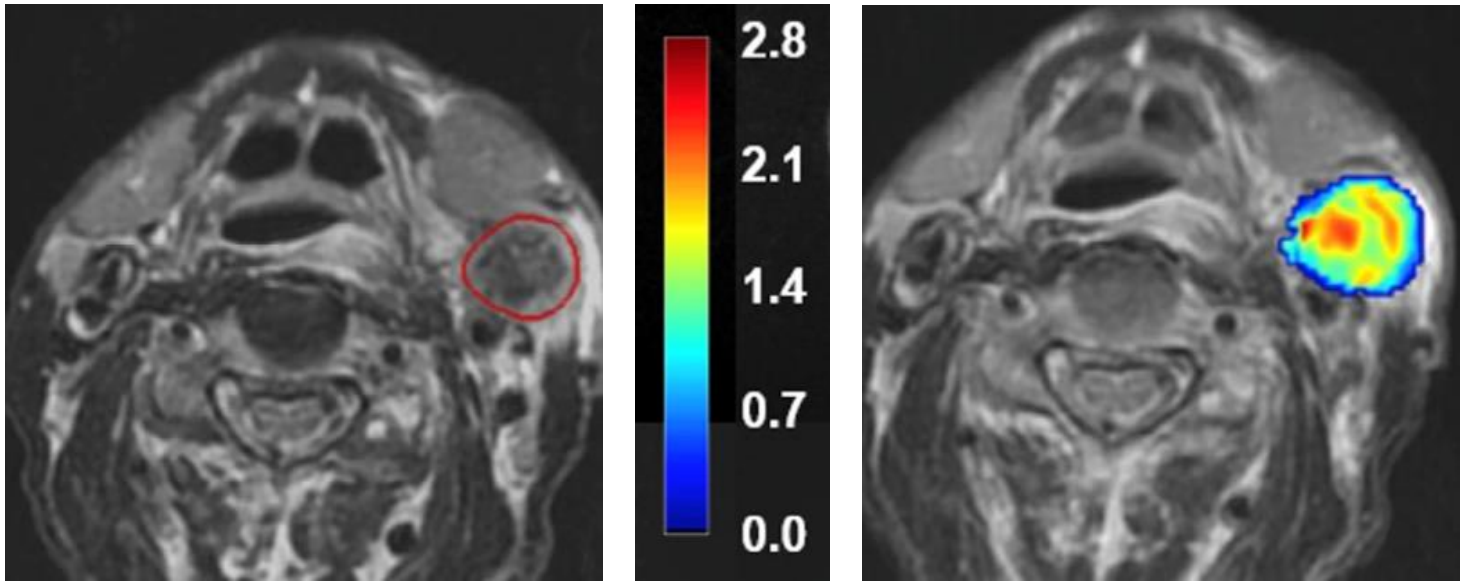
Extraction of
Non Semantic features

texture analysis is used to quantify

tumor heterogeneity → ***prediction of response***

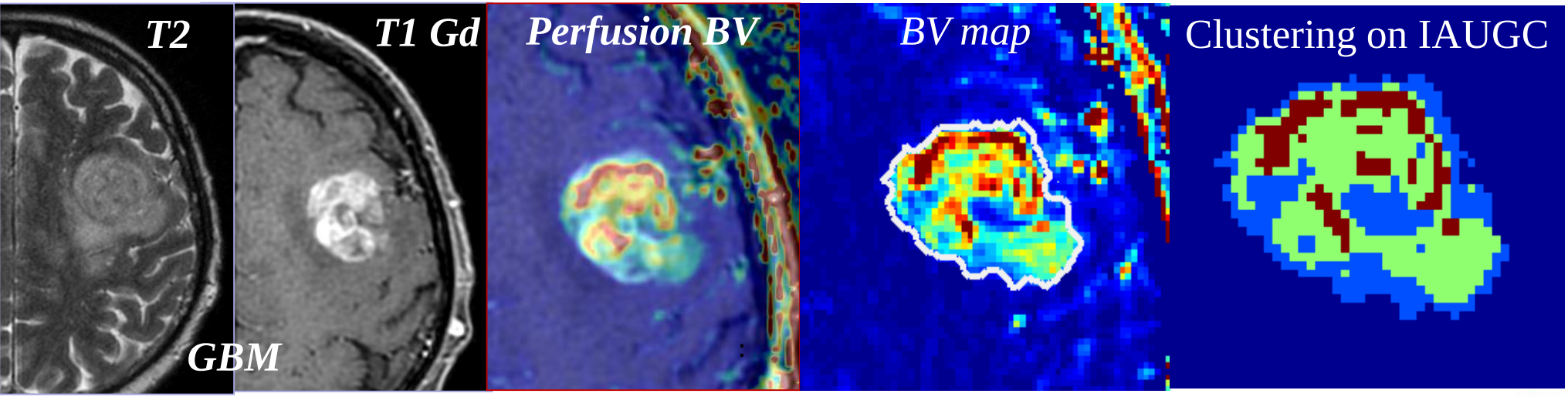


Extraction of
Non Semantic features

texture analysis is used to quantify

tumor heterogeneity → ***prediction of response***

Perfusion DCE with volumetric analysis



tumor heterogeneity

IAUGC levels

low

intermediate

high

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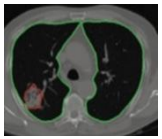
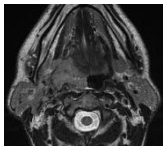
CT - MRI



CT attenuation

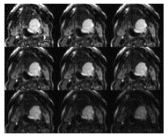


MR signal intensity

- morphologycal data
- non-morphologycal data

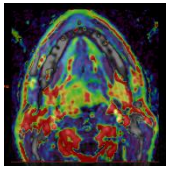
multiple surrogate biomarkers of tumor

can be combined from clinical information to omics technologies



Diffusion MR → *cellularity*

ADC - D - f – D - K – Dk -*



Perfusion CT/MR → *vascularity*

BV - BF – Ktrans – Ve- Kep - Vp

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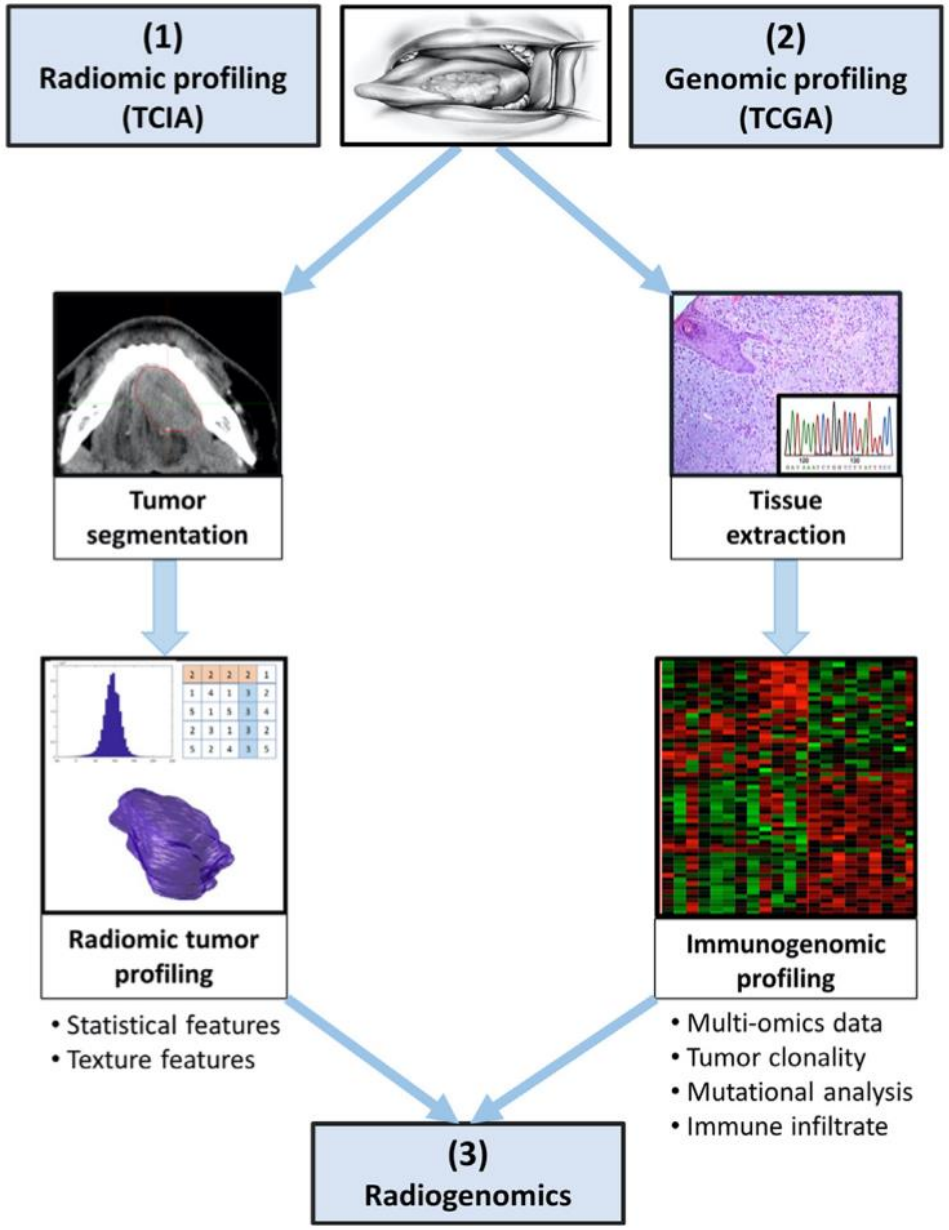

Radiogenomics

field of research aimed at developing tools for non-invasive genotyping by identifying imaging biomarkers for genomic subtypes

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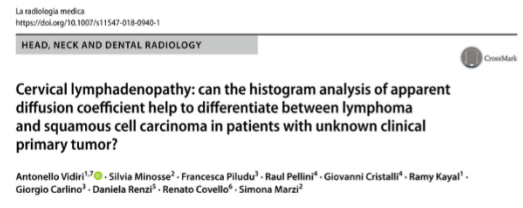
Radiomics *is designed to be used in decision support of* ***precision medicine***

- ✓ ***uses standard of care images*** that are routinely acquired in clinical practice, it presents a cost-effective and highly feasible addition for supporting clinical decisions;
- ✓ ***non-invasively*** characterizes 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;
- ✓ ***produces*** prognostic and/or predictive biomarker value derived from routine, standard of care imaging data;
- ✓ ***allows*** fast, low-cost, and repeatable means for longitudinal monitoring.

MRI

characterization

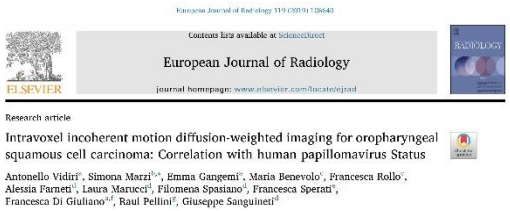
prediction to response to treatment


La radiologia medica
https://doi.org/10.1007/s11547-018-0940-1

HEAD, NECK AND DENTAL RADIOLOGY

Cervical lymphadenopathy: can the histogram analysis of apparent diffusion coefficient help to differentiate between lymphoma and squamous cell carcinoma in patients with unknown clinical primary tumor?

Antonello Vidiri[1,7] · Silvia Minosse[2] · Francesca Piludu[3] · Raul Pellini[4] · Giovanni Cristalli[4] · Ramy Kayal[5] · Giorgio Carlino[3] · Daniela Renzi[2] · Renato Covello[6] · Simona Marzi[2]


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[a], Alessia Farneti[a], Laura Marucci[d], Filomena Spasiano[b], Francesca Sperati[a], Francesca Di Giuliano[a,f], Raul Pellini[g], Giuseppe Sanguineti[g]

MRI-based Radiomics to Differentiate Benign and Malignant Parotid Tumors with External Validation.

Submitted AJNR


Contents lists available at ScienceDirect

European Journal of Radiology

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

Research papers

The prediction of the treatment response of cervical nodes using intravoxel incoherent motion diffusion-weighted imaging

Simona Marzi[a,*], Francesca Piludu[b], Giuseppe Sanguineti[c], Laura Marucci[c], Alessia Farneti[c], Irene Terrenato[d], Raul Pellini[e], Maria Benevolo[f], Renato Covello[f], Antonello Vidiri[b]


frontiers

Comparison of Machine Learning Classifiers to Predict Patient Survival and Genetics of GBM: Towards a Standardized Model for Clinical Implementation

Luca Pasquini[1,2], Antonio Napolitano[3], Martina Lucignani[3], Emanuela Tagliente[3], Francesco Dellepiane[2], Maria Camilla Rossi-Espagnet[2,4], Matteo, Ritrovato[5], Antonello Vidiri[6], Veronica Villani[7], Giulio Ranazzi[8], Antonella Stoppacciaro[8], Andrea Romano[2], Alberto Di Napoli[2,9], Alessandro Bozzao[2]


Contents lists available at ScienceDirect

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

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Differentiation between benign and malignant parotid lesions

MRI-based Radiomics to Differentiate between Benign and Malignant Parotid Tumors with External Validation

Authors: Francesca Piludu[1], Simona Marzi[2], Marco Ravanelli[3], Raul Pellini[4], Renato Covello[5], Irene Terrenato[6], Davide Farina[3], Riccardo Campora[3], Valentina Ferrazzoli[1], Antonello Vidiri[1]

Submitted AJNR

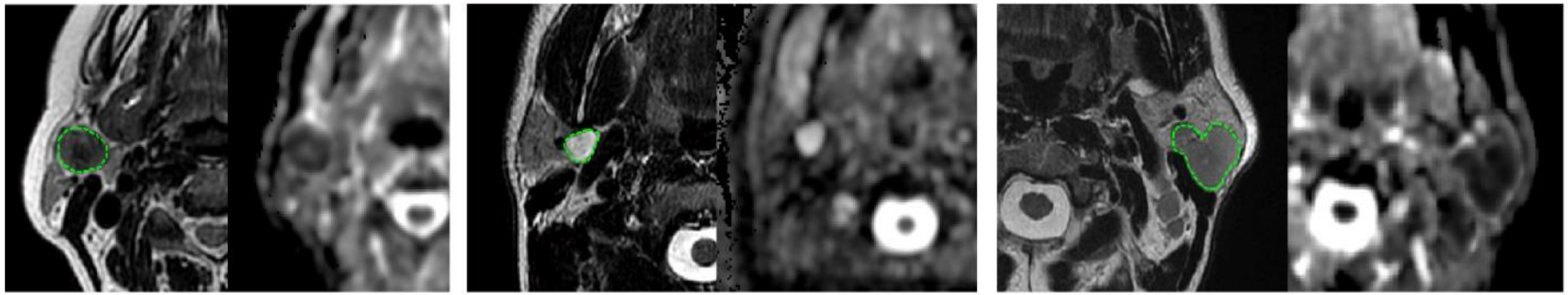
Texture analysis - MRI:

✓morphological characteristics (type of margins and contrast enhancement)

✓T2 signal intensity

✓ADC maps (DWI)

with external validation (Department of Radiology, University of Brescia)



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Differentiation between benign and malignant parotid lesions

Feature Family

Morphological	*IntensityHistogram*	*IntensityVolumeHistogram*	*GLGM*	*IntensityDirect*
Volume	*Mean*	*VolumeIntFract_10*	*JointMaximum*	*GlobalEntropy*
ApproximateVolume	*Variance*	*VolumeIntFract_90*	*JointAverage*	*GlobalMean*
SurfaceArea	*Skewness*	*IntensityVolFract_10*	*JointVariance*	*GlobalMedian*
SurfaceToVolumeRatio	*Kurtosis*	*IntensityVolFract_90*	*JointEntropy*	*InterQuartileRange*
Compactness1	*Median*	*VolumeFractionDiff*	*DifferenceAverage*	*Kurtosis*
Compactness2	*Min*	*IntensityFractDiff*	*DifferenceVariance*	*Skewness*
SphericalDisproportion	*10thPercentile*	*AreaUnderIVHCurve*	*DifferenceEntropy*	*0.25Quantile*
Sphericity	*90thPercentile*		*SumAverage*	*0.75Quantile*
Asphericity	*Max*		*SumVariance*	
CentreOfMassShift	*Mode*		*SumEntropy*	
Maximum3DDiameter	*InterQuartileRange*		*AngularSecondMoment*	
MajorAxisLength	*Range*		*Contrast*	
MinorAxisLength	*MeanAbsoluteDeviation*		*Dissimilarity*	
…	…	…	…	…

Authors: Francesca Piludu[1], Simona Marzi[2], Marco Ravanelli[3], Raul Pellini[4], Renato Covello[5], Irene Terrenato[6], Davide Farina[3], Riccardo Campora[3], Valentina Ferrazzoli[1], Antonello Vidiri[1]

Differentiation between benign and malignant parotid lesions

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CentreOfMassShift	*Mode*		*SumEntropy*	
Maximum3DDiameter	*InterQuartileRange*		*AngularSecondMoment*	
MajorAxisLength	*Range*		*Contrast*	
MinorAxisLength	*MeanAbsoluteDeviation*		*Dissimilarity*	
…	…	…	…	…

.... but only 4 features have been selected to build the models using statistical tests and / or dedicated algorithms

MRI-based Radiomics to Differentiate between Benign and Malignant Parotid Tumors with External Validation

Authors: Francesca Piludu[1], Simona Marzi[2], Marco Ravanelli[3], Raul Pellini[4], Renato Covello[5], Irene Terrenato[6], Davide Farina[3], Riccardo Campora[3], Valentina Ferrazzoli[1], Antonello Vidiri[1]

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Differentiation between benign and malignant parotid lesions

End-point	Selected Features	Accuracy(%)	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)
Warthin's vs Malignant tumors	***ADC P25*** ***Volume Density AEE*** **Margins** **Gd**	**86.7** [73.2, 95.0]	87.5 [71.0, 96.5]	84.6 [54.5,98.1]	93.3 [79.5, 98.1]	73.3 [51.7, 87.6]
Benign* vs Warthin's tumors	***ADC P25*** ***Volume Density AEE*** ***MinimumHistogramGradient*** **Gd**	**91.9** [78.1, 98.3]	84.6 [54.6, 98.1]	95.8 [78.9, 99.9]	91.7 [61.4, 98.7]	92.0 [76.2, 97.6]
Benign* vs Malignant tumors	***ADC P25*** ***T2 P10*** **Gd** **Margins**	**80.4** [67.6, 89.8]	84.4 [67.2, 94.7]	75.0 [53.3, 90.2]	81.8 [68.9, 90.1]	78.2 [60.9, 89.3]

Table. Predictive Performance of the three models on the training cohort

Differentiation between benign and malignant parotid lesions

End-point	Selected Features	Accuracy(%)	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)
Warthin's vs Malignant tumors	***ADC P25*** ***Volume Density AEE*** **Margins** **Gd**	**77.8** [57.7,91.4]	90.0 [68.3,98.8]	42.9 [9.9,81.6]	81.0 [68.6,89.2]	60 [23.8, 87.8]
Benign* vs Warthin's tumors	***ADC P25*** ***Volume Density AEE*** ***MinimumHistogramGradient*** **Gd**	**91.7** [73.0,99.0]	85.7 [42.1,99.6]	94.1 [71.3, 99.9]	85.7 [46.7,97.6]	94.1 [72.2, 99.9]
Benign* vs Malignant tumors	***ADC P25*** ***T2 P10*** **Gd** **Margins**	**80.4** [67.6, 89.8]	84.4 [67.2, 94.7]	75.0 [53.3, 90.2]	81.8 [68.9, 90.1]	78.2 [60.9, 89.3]

Table. Predictive Performance of the three models on the validation cohort

MRI-based Radiomics to Differentiate between Benign and Malignant Parotid Tumors with External Validation

Authors: Francesca Piludu[1], Simona Marzi[2], Marco Ravanelli[3], Raul Pellini[4], Renato Covello[5], Irene Terrenato[6], Davide Farina[3], Riccardo Campora[3], Valentina Ferrazzoli[1], Antonello Vidiri[1]

....with similar performance

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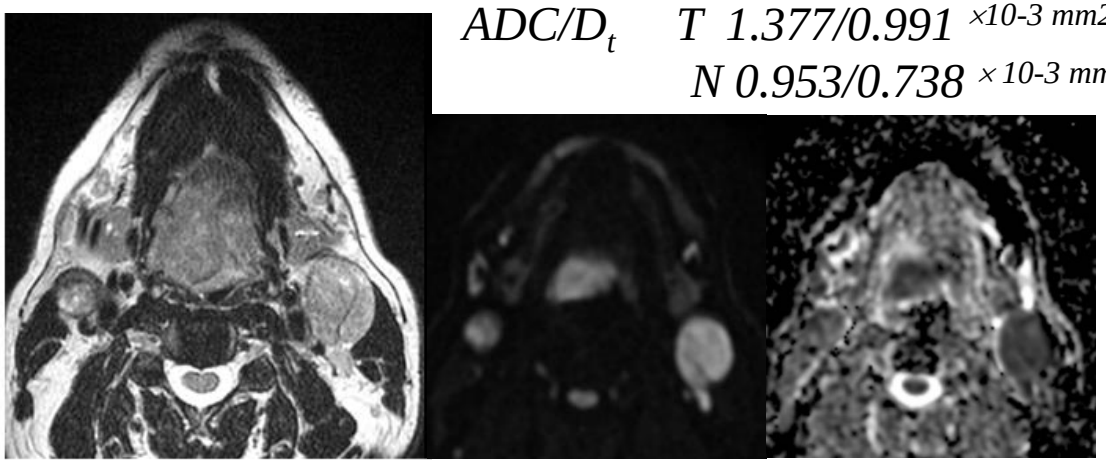
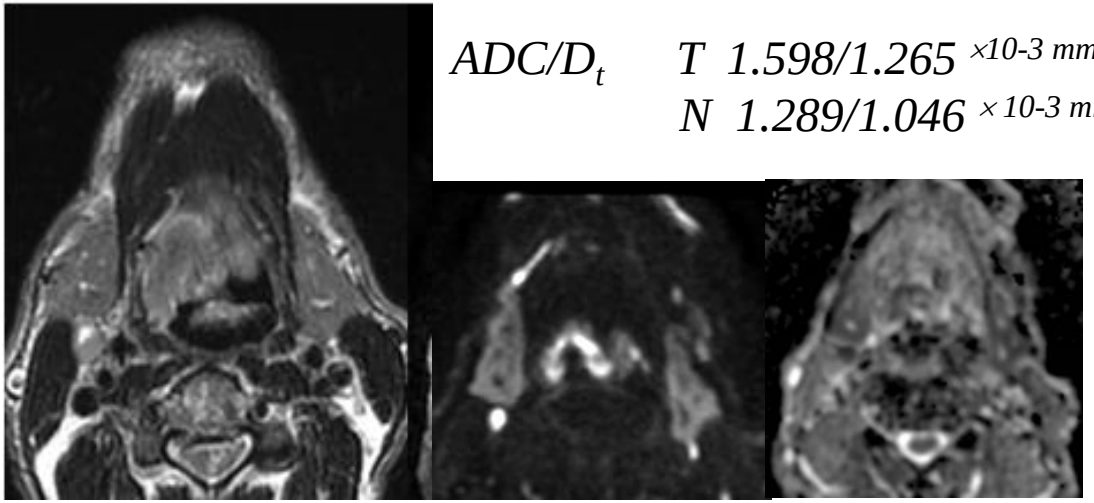
MRI for Prediction HPV status in Oropharyngeal SCC



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*

European Journal of Radiology 119 (2019) 108640

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Research article

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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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MRI for Prediction of tumor response to CHT-RT in head-neck nodes

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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

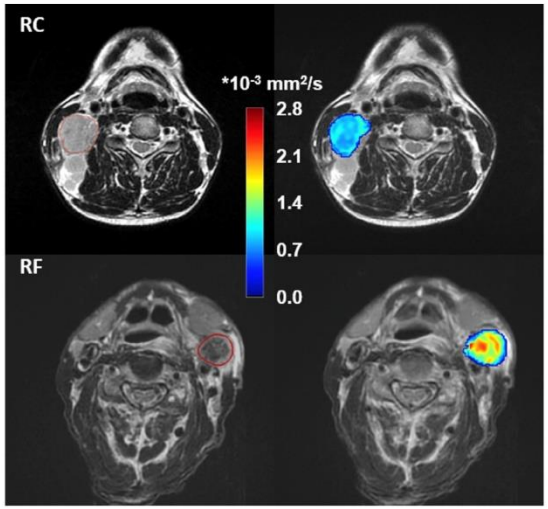
Elisa Scalco [a,*,1], Simona Marzi [b,1], Giuseppe Sanguineti [c], Antonello Vidiri [d], Giovanna Rizzo [a]

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)*



Texture analysis

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%)

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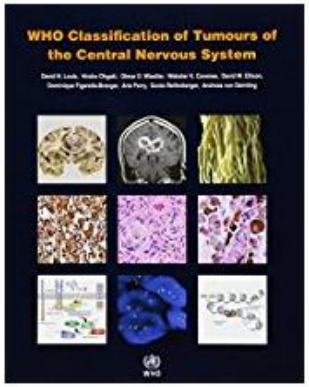
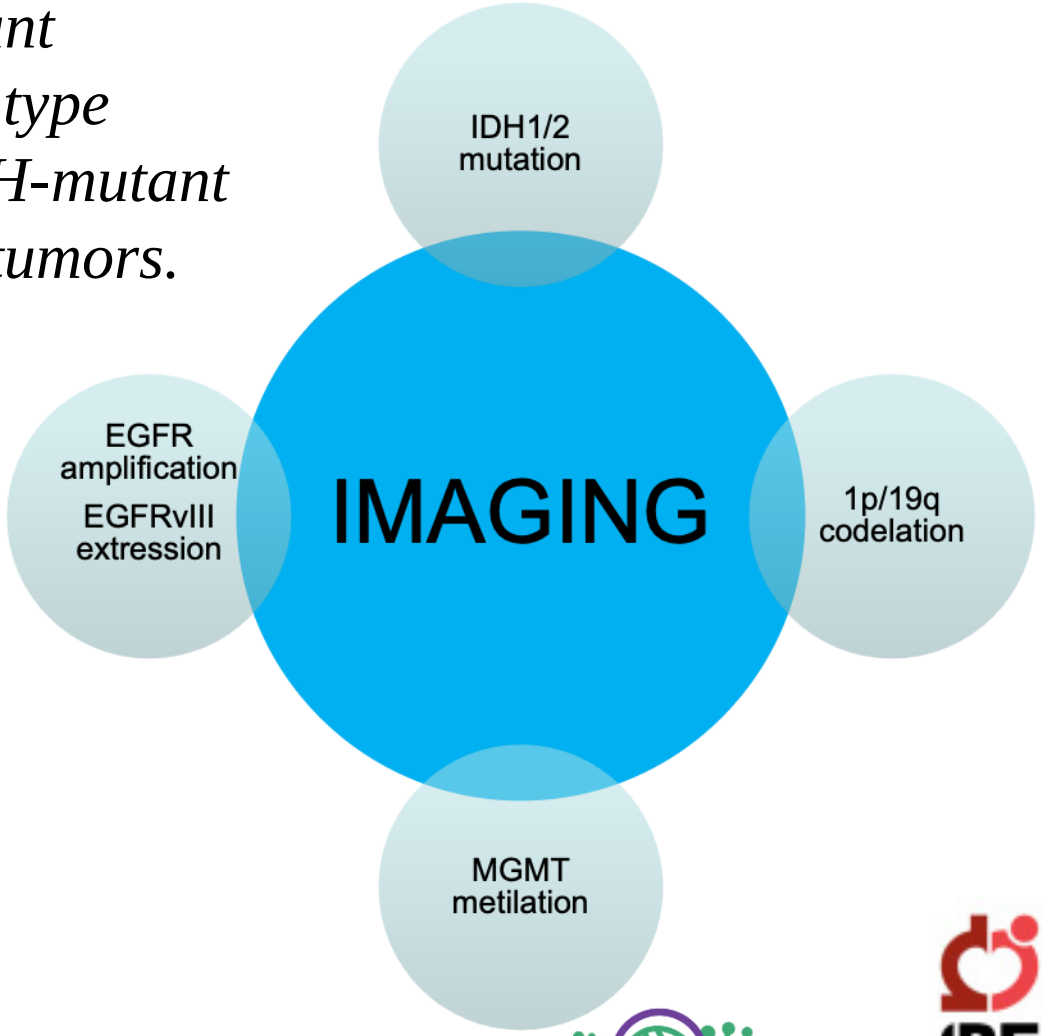
correlation between imaging - molecular date – genetic alterations



in 2016 WHO grade II and III infiltrating gliomas

- *astrocytoma IDH-mutant*
- *astrocytoma IDH-wild type*
- *oligodendroglioma IDH-mutant 1p/19q codeleted tumors.*

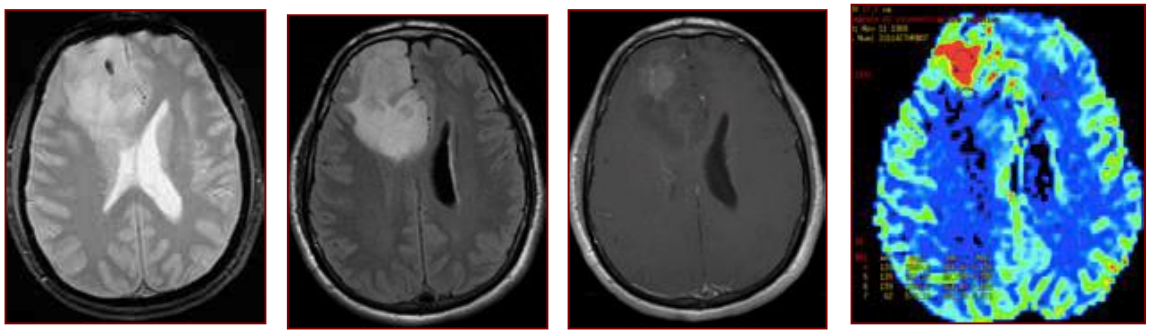
genomic alterations in gliomas are associated with a number of radiographic features on MRI



correlation between imaging - molecular date – genetic alterations

GLIOMA PROJECT

correlation



molecular features

- ✓ *IDH mutation,*
- ✓ *MGMT*
- ✓ *Ki-67*
- ✓ *EGFR*

MRI…pre treatment

- ✓ *morphologycal imaging (site, signal intensity, margin, contrast enhancement, mismacth between T2 and FLAIR)*
- ✓ *non morphological imaging (Diffusion and Perfusion)*

frontiers

Comparison of Machine Learning Classifiers to Predict Patient Survival and Genetics of GBM: Towards a Standardized Model for Clinical Implementation

Luca Pasquini[1,2], Antonio Napolitano[3], Martina Lucignani[3], Emanuela Tagliente[3], Francesco Dellepiane[2], Maria Camilla Rossi-Espagnet[2,4], Matteo, Ritrovato[5], Antonello Vidiri[6], Veronica Villani[7], Giulio Ranazzi[8], Antonella Stoppacciaro[8], Andrea Romano[2], Alberto Di Napoli[2,9], Alessandro Bozzao[2]

[1]Neuroradiology Unit, Radiology Department, Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA.
[2]Neuroradiology Unit, NESMOS Department, Sant'Andrea Hospital, La Sapienza University, Via di Grottarossa 1035, Rome 00189, Italy.
[3]Medical Physics Department, Bambino Gesù Children's Hospital, IRCCS, Piazza di Sant'Onofrio, 4, Rome 00165, Italy.
[4]Neuroradiology Unit, Imaging Department, Bambino Gesù Children's Hospital, IRCCS, Piazza di Sant'Onofrio, 4, Rome 00165, Italy.
[5]Unit of HTA, Biomedical Technology Risk Manager, Bambino Gesù Children's Hospital, IRCCS, Piazza di Sant'Onofrio, 4, Rome 00165, Italy.
[6]Radiology and Diagnostic Imaging Department, Regina Elena National Cancer Institute, IRCCS, Via Elio Chianesi 53, Rome 00144, Italy.
[7]Neuro-Oncology Unit, Regina Elena National Cancer Institute, IRCCS, Via Elio Chianesi 53, Rome 00144, Italy.
[8]Department of Clinical and Molecular Medicine, Surgical Pathology Units , Sant'Andrea Hospital, La Sapienza University, Via di Grottarossa 1035, Rome 00189, Italy.
[9]Radiology Department, Castelli Romani Hospital, Via Nettunense Km 11.5, Ariccia 00040, Rome, Italy.

multicentric study

156 adult patients with pathologic diagnosis of GBM

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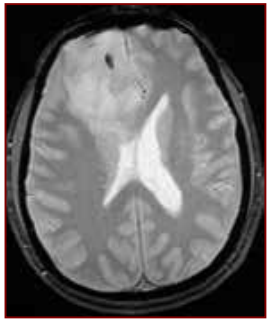
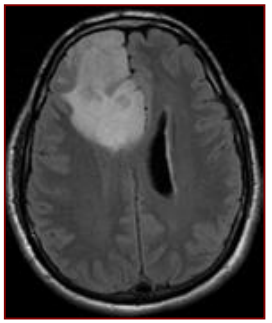
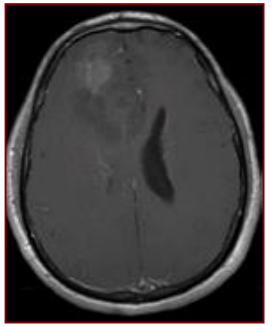
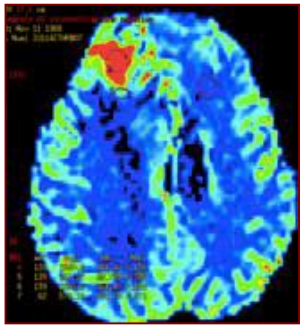
correlation between imaging - molecular date – genetic alterations

GLIOMA PROJECT

correlation

molecular features
- ✓ *IDH mutation,*
- ✓ *MGMT*
- ✓ *Ki-67*
- ✓ *EGFR*

MRI…pre treatment
- ✓ *morphologycal imaging (site, signal intensity, margin, contrast enhancement, mismacth between T2 and FLAIR)*
- ✓ *non morphological imaging (Diffusion and Perfusion)*

accuracy

- ✓ OS (74.5%) - **textural features from FLAIR /T2 / necrosis**
- ✓ IDH mutation (98%) – **rCBV on perfusion**
- ✓ MGMT methylation (81.5%) – **FLAIR sequences**
- ✓ Ki-67 expression (95%) – **diffusion ADC**
- ✓ EGFR amplification (93%) – **rCBV on perfusion / T2 sequences**


frontiers

Comparison of Machine Learning Classifiers to Predict Patient Survival and Genetics of GBM: Towards a Standardized Model for Clinical Implementation

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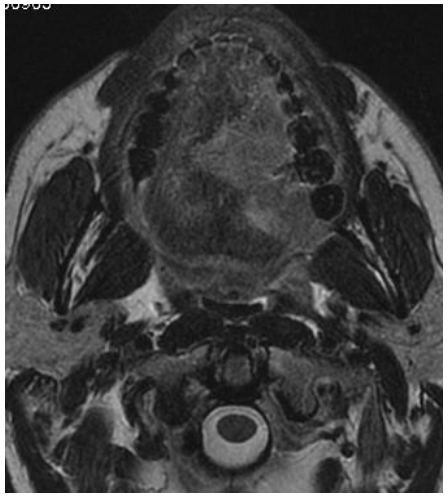
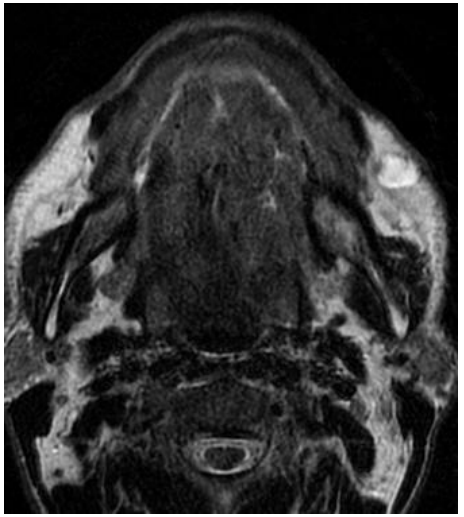
Ongoing studies

- ✓ *correlation between radiomics features in patients with **lung tumors** underwent surgery and specific driver mutational status*
- ✓ *correlation between the parameters identified by perfusion imaging (neo-vascularization) and diffusion (cellularity and stroma) with those of the immunohistochemistry and digital pathology, RNASEQ, and with the immunoprofiling of the cells of the immune system in the periphery in **head and neck tumors***
- ✓ *radiomics features in **cervical cancer** underwent radio-chemiotherapy and overall survival*
- ✓ *radiomics features in **liver** metastases underwent chemiotherapy and surgery*

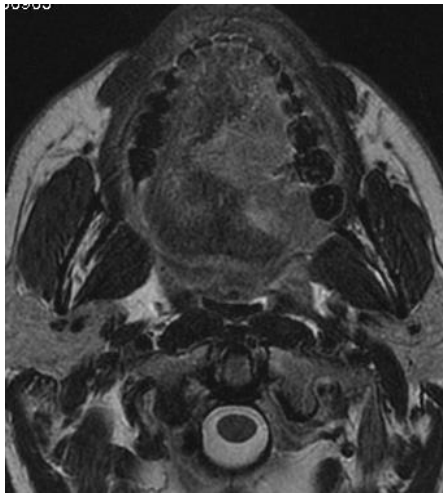
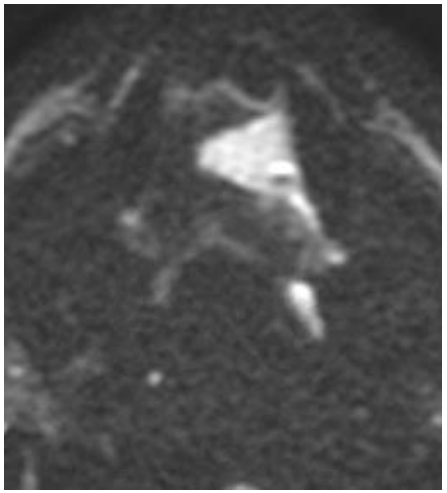
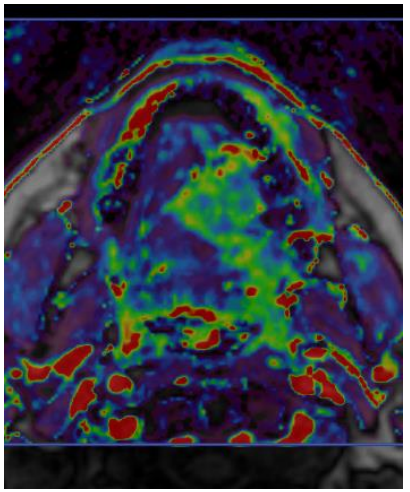
correlation: imaging parameters - immunohistochemistry - digital pathology



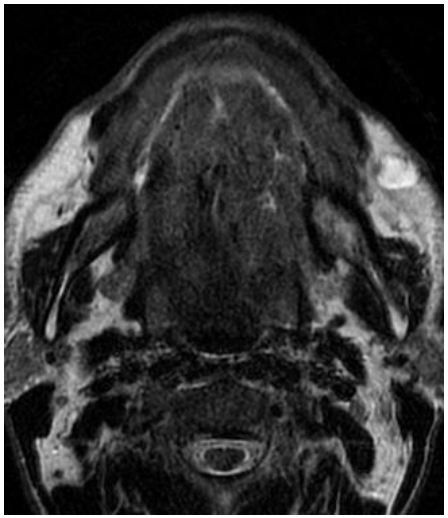
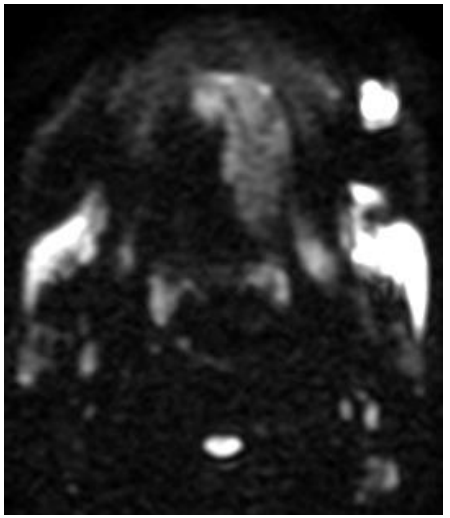
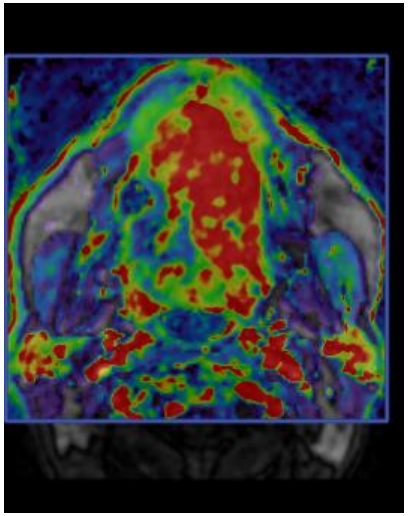
Tongue SCC MRI T2



correlation: imaging parameters - immunohistochemistry - digital pathology

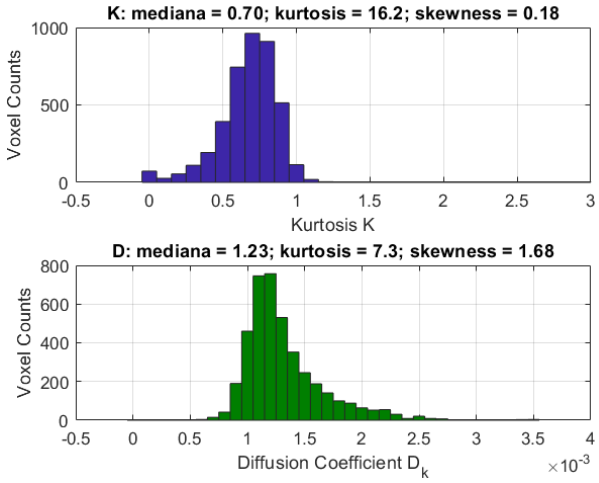





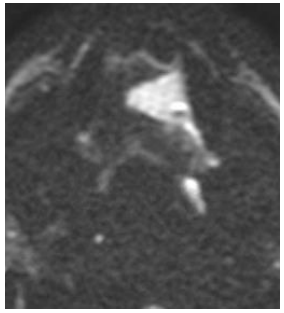
Tongue SCC MRI T2 diffusion perfusion

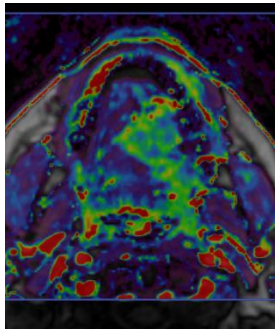





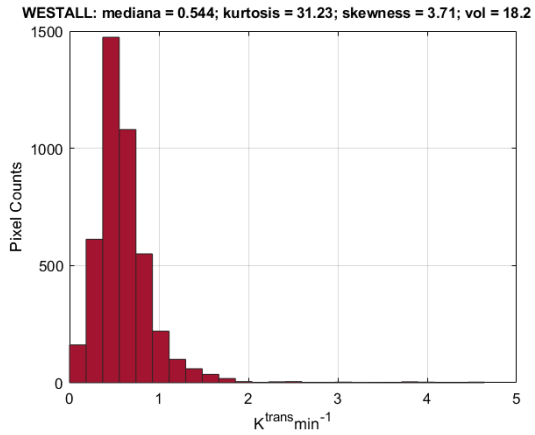
diffusion and perfusion MR related to tissue architecture 4thNov2020 ISAB IRE

correlation: imaging parameters - immunohistochemistry - digital pathology





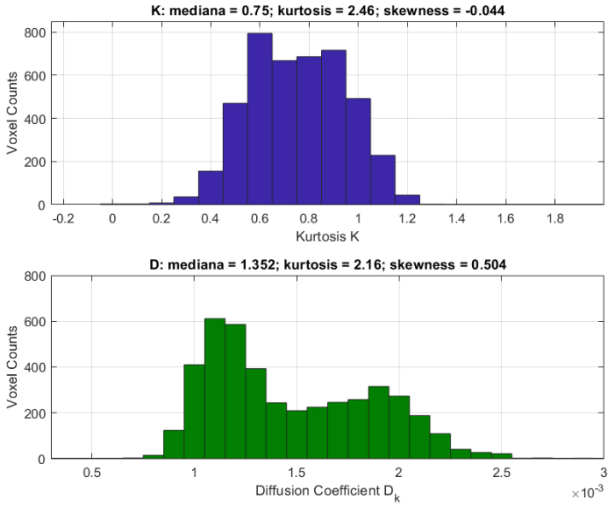


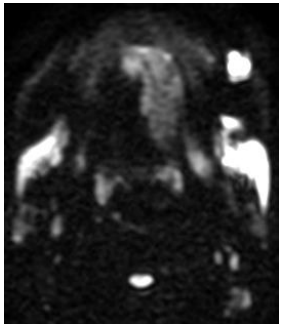


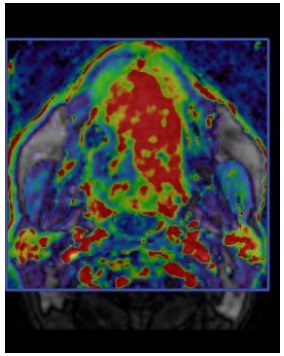
diffusion

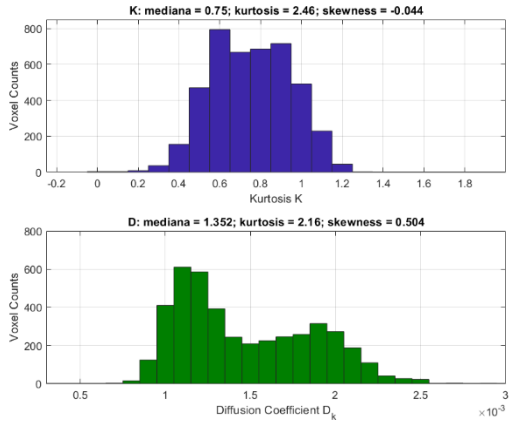
quantitative evaluation of whole tumor with histogram analysis

perfusion





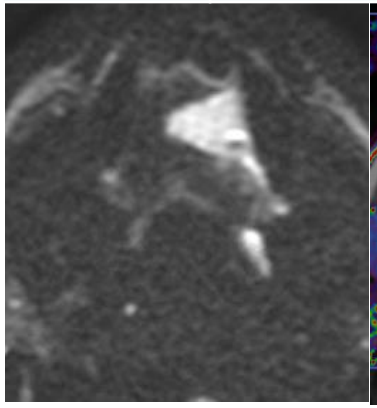


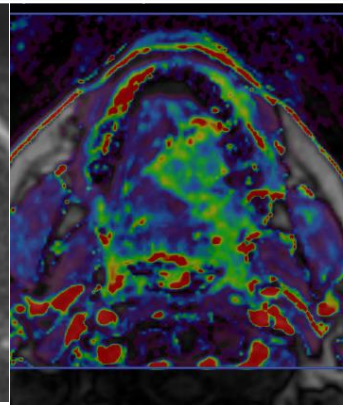


diffusion and perfusion MR related to tissue architecture 4thNov2020 ISAB IRE

correlation: imaging parameters - immunohistochemistry - digital pathology

Ktrans(min-1)	Kep(min-1)	ve(f.u.)	IAUGC90(a.u.)	MaxSlope(s-1)	CE(a.u.)	BAT(s)	D	K	Vol(cm3)
0,544	1,12	0,517	0,51	0,08	3,37	14,0	1,230	0,700	18,3





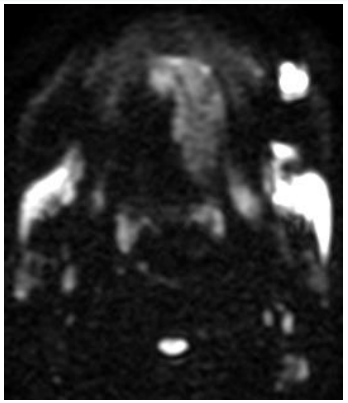
CD4	60%	3+
CD8	40%	3+
CD20	30%	3+
PDL1	5%	1+
COLL IV	10%	1+
Fibronectin	90%	3+
CD3	70%	3+
Mena WT	90%	2+

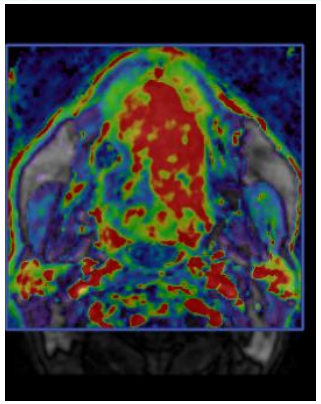
himmunoistochemical

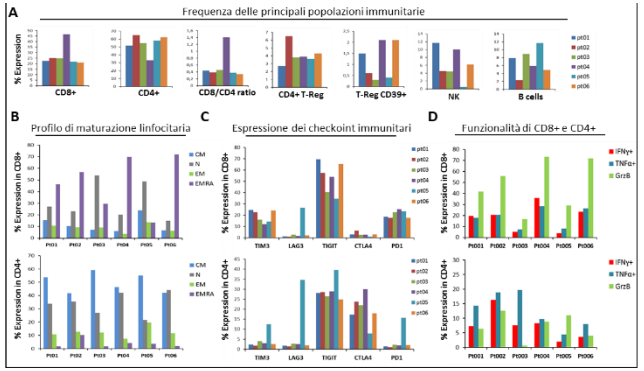
Immuno monitoring
Belinda Palermo
Maria Angela Panetta

we are working to correlate….. **what implications ?**

Ktrans(min-1)	Kep(min-1)	ve(f.u.)	IAUGC90(a.u.)	MaxSlope(s-1)	CE(a.u.)	BAT(s)	D	K	Vol(cm3)
1,464	1,92	0,791	1,08	0,16	5,61	27,5	1,352	0,750	26,3







digital pathology

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correlation: imaging parameters - immunohistochemistry - digital pathology

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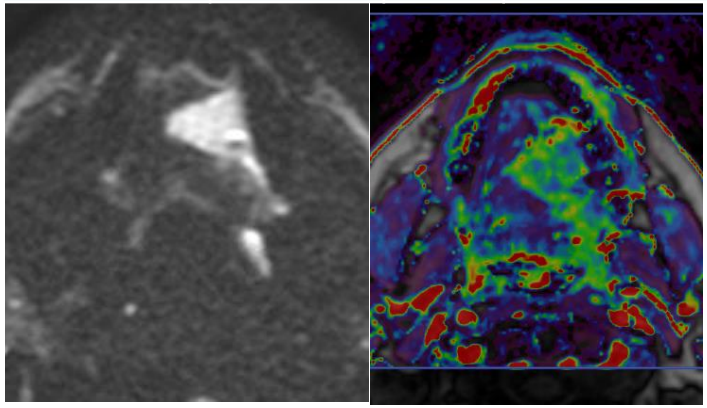


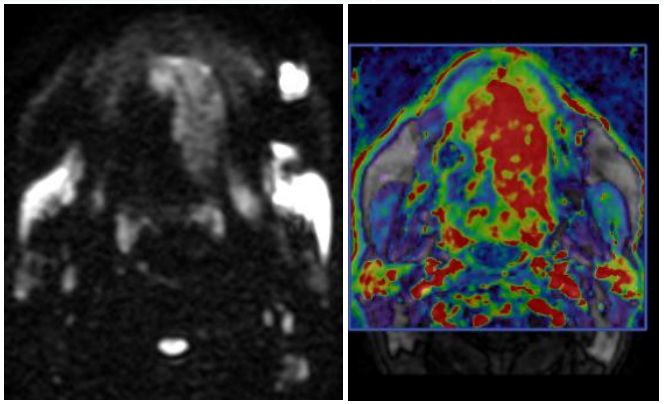
CD4	60%	3+
CD8	40%	3+
CD20	30%	3+
PDL1	5%	1+
COLL IV	10%	1+
Fibronectin	90%	3+
CD3	70%	3+
Mena WT	90%	2+

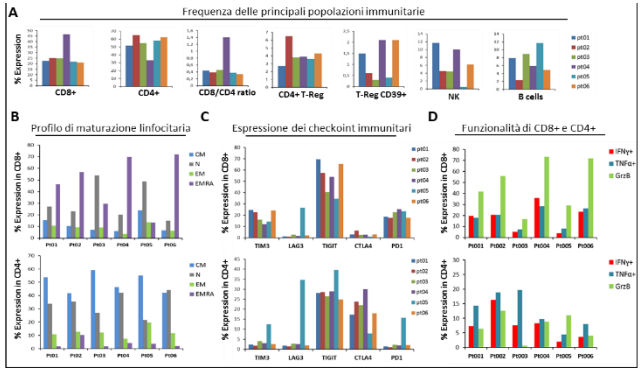
himmunoistochemical

Immuno monitoring
Belinda Palermo
Maria Angela Panetta

....the possibility to identify with radiogenomic approach a panel of baseline imaging biomarkers before surgery that can be used to define prognostic and diagnostic markers

Ktrans(min-1)	Kep(min-1)	ve(f.u.)	IAUGC90(a.u.)	MaxSlope(s-1)	CE(a.u.)	BAT(s)	D	K	Vol(cm3)
1,464	1,92	0,791	1,08	0,16	5,61	27,5	1,352	0,750	26,3





digital pathology

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Work Flow

cancer patients

cancer imaging

RX/MX/US/CT/MR/PET-CT

contain information that reflects tumor biology

combining date

imaging biomarkers from radiomics patient characteristics

age- sex- lifestyle habits – genomic date

develop support tool

deep learning – machine learning – artificial intelligence

clinical practice

guide the management of patients at bedside

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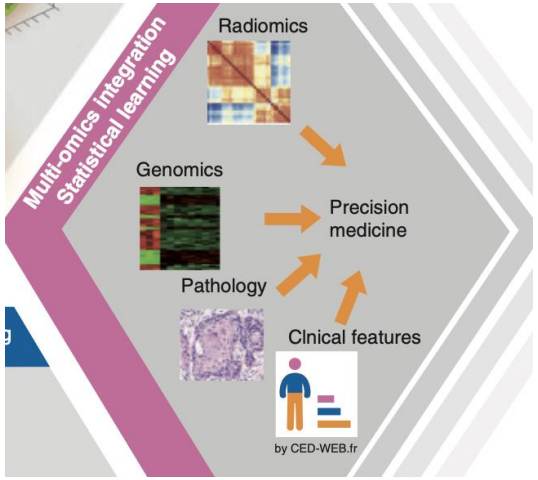
CONCLUSION

Radiomics has

- ✓ immense potential to improve knowledge in tumor biology
- ✓ allows tumor monitoring across time, with images being routinely acquired throughout the course of treatment
- ✓ imaging biomarkers may be used to cancer detection, diagnosis, choice of therapeutic strategy, prognosis inference, prediction of response.



still a long way to go, like any challenge

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to my Unit

Medical Physics Laboratory

UNIT of Head Neck Surgery
UNIT of Radiotherapy
UNIT of Tumor Immunology and Immunotherapy
UOSD Biostatistics, Bioinformatics and Clinical Trial Center
UOSD SAFU
UNIT of Pathology
UNIT of Neuroncology

….and to you for our attention

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