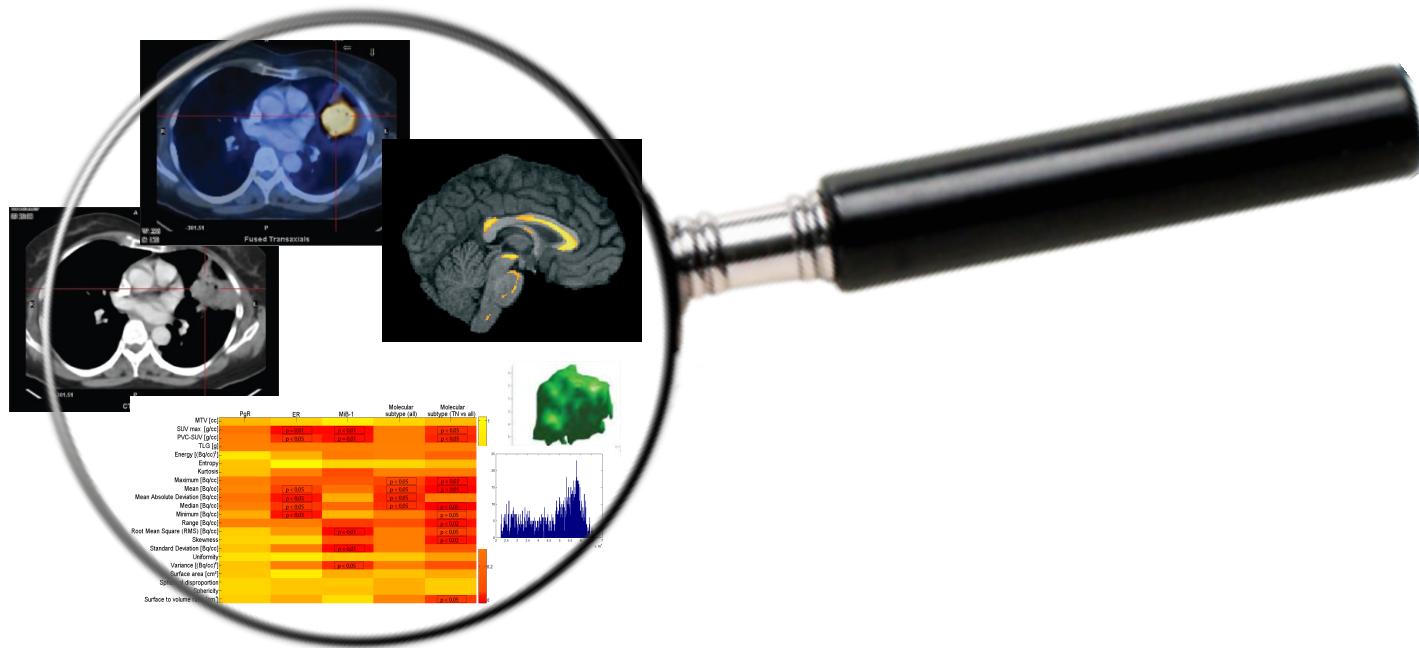


Radiomics and radiogenomics in cancer



Isabella Castiglioni

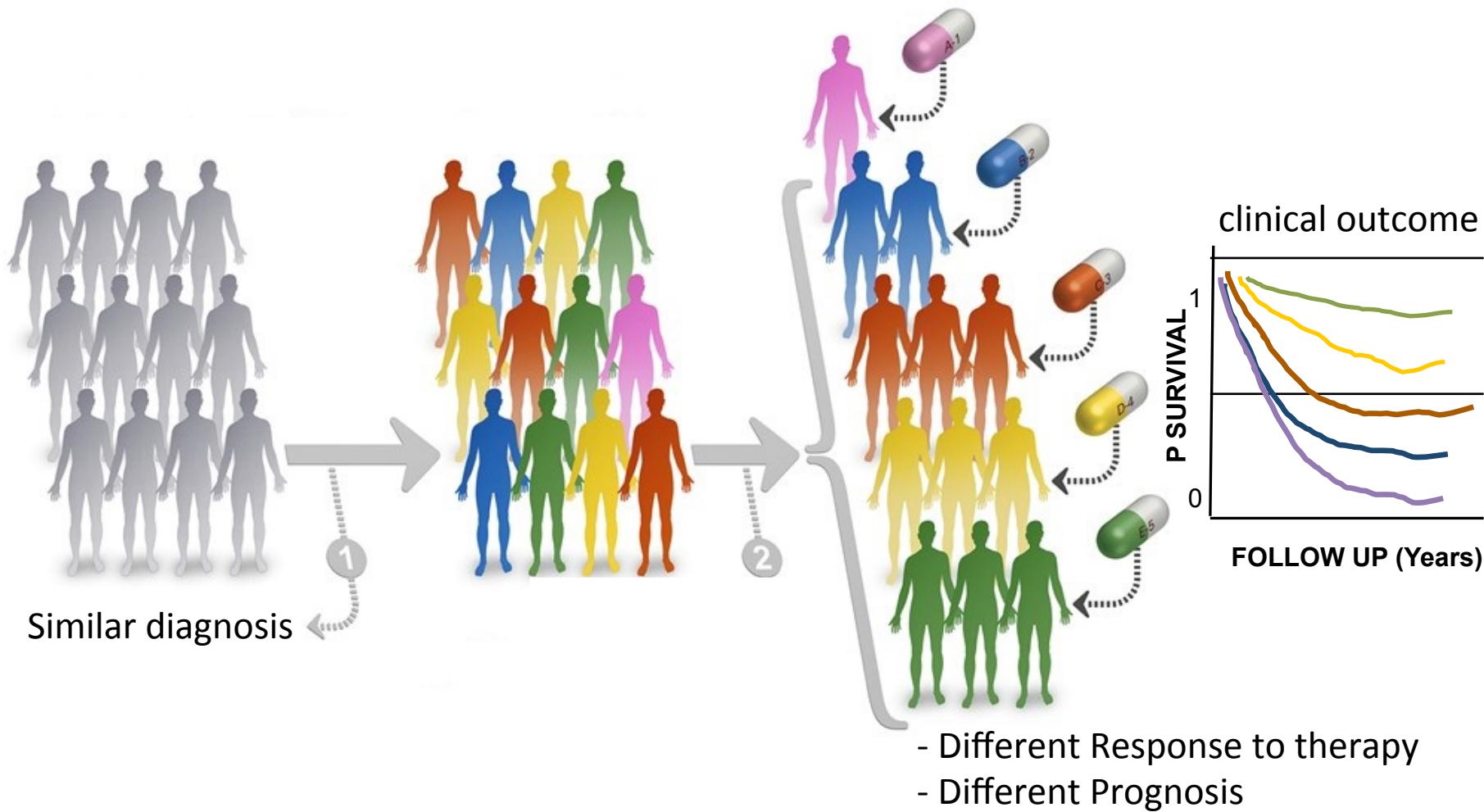
*Institute of Molecular Bioimaging and Physiology –
National Research Council (IBFM-CNR)
Segrate (Mi), Italy*



INLAB[®]

Current challenges of personalized medicine

DISEASE HETEROGENEITY



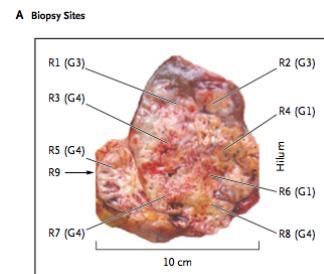
Can genomics identify subtypes?

INTRA-TUMOUR HETEROGENEITY AND TUMOR BIOPSY

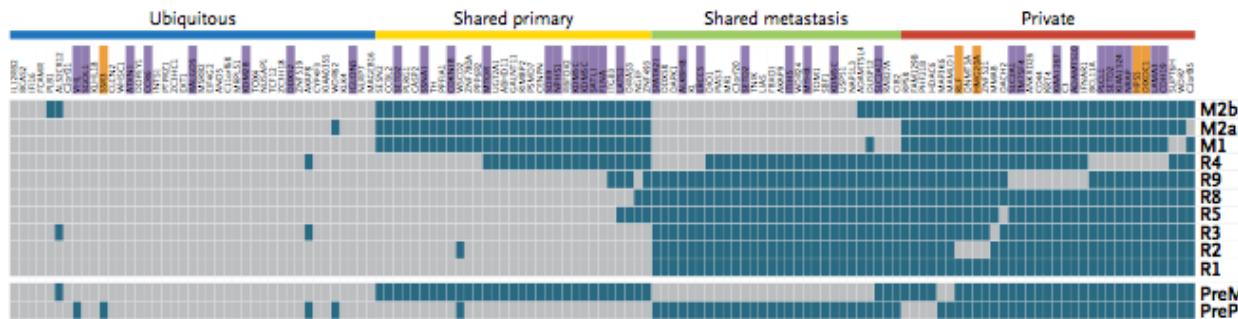


Intratumor Heterogeneity and Branched Evolution Revealed by Multiregion Sequencing

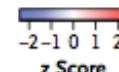
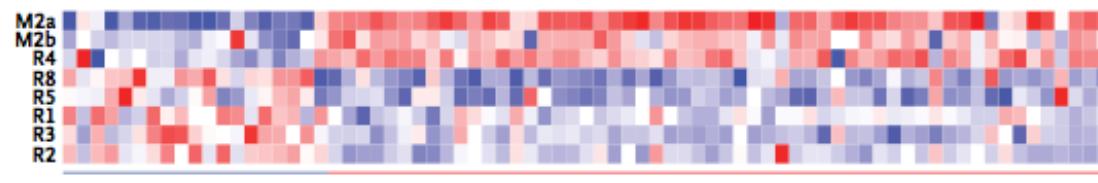
Marco Gerlinger, M.D., Andrew J. Rowan, B.Sc., Stuart Horswell, M.Math., James Larkin, M.D., Ph.D., David Endesfelder, Dip.Math., Eva Gronroos, Ph.D., Pierre Martinez, Ph.D., Nicholas Matthews, B.Sc., Aengus Stewart, M.Sc., Patrick Tarpey, Ph.D., Ignacio Varela, Ph.D., Benjamin Phillipsmore, B.Sc., Sharmin Begum, M.Sc., Neil Q. McDonald, Ph.D., Adam Butler, B.Sc., David Jones, M.Sc., Keiran Raine, M.Sc., Calli Latimer, B.Sc., Claudio R. Santos, Ph.D., Mahrokh Nohadani, H.N.C., Aron C. Eklund, Ph.D., Bradley Spencer-Dene, Ph.D., Graham Clark, B.Sc., Lisa Pickering, M.D., Ph.D., Gordon Stamp, M.D., Martin Gore, M.D., Ph.D., Zoltan Szallasi, M.D., Julian Downward, Ph.D., P. Andrew Futreal, Ph.D., and Charles Swanton, M.D., Ph.D.



B Regional Distribution of Mutations



C Prognostic Signature Genes



Can in vivo 3D imaging of lesions
capture such heterogeneity?

Radiomics: a new approach for the study of cancer



HHS Public Access

Author manuscript

Eur J Cancer. Author manuscript; available in PMC 2015 August 12.

Published in final edited form as:

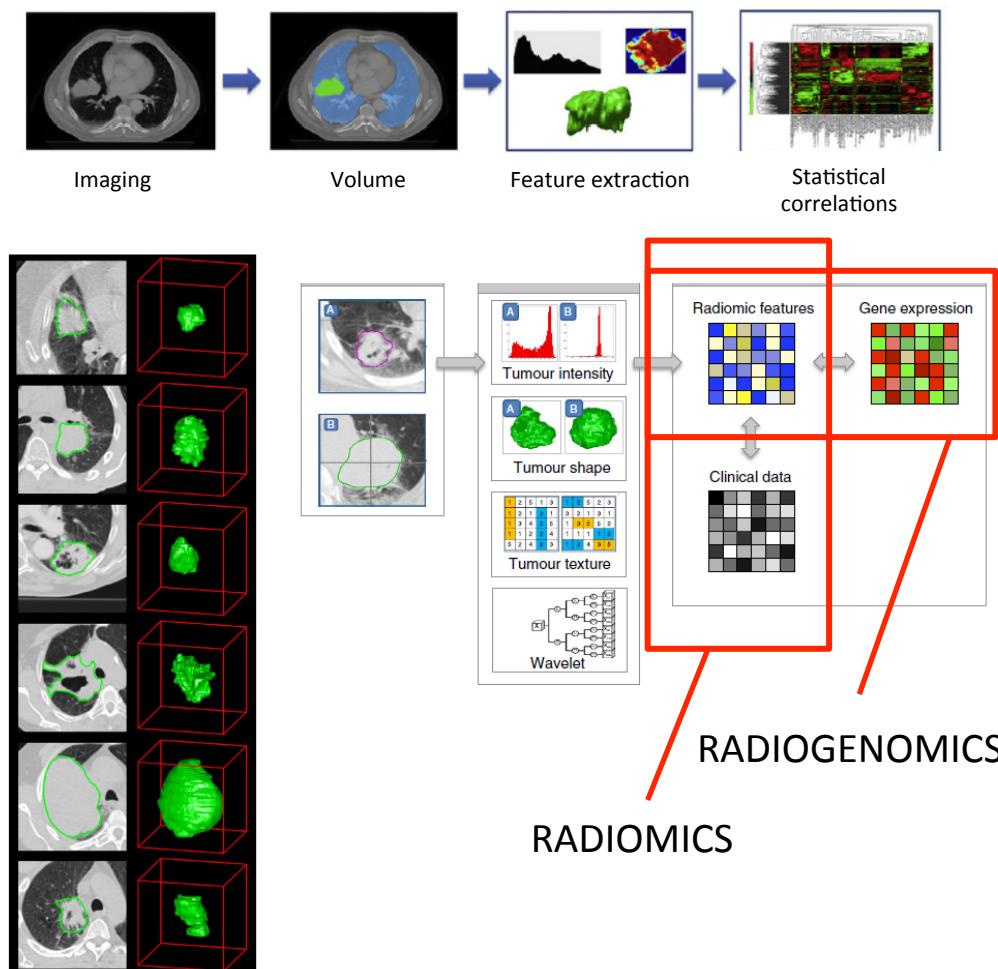
Eur J Cancer. 2012 March ; 48(4): 441–446. doi:10.1016/j.ejca.2011.11.036.

Radiomics: Extracting more information from medical images using advanced feature analysis

Philippe Lambin^{a,*}, Emmanuel Rios-Velazquez^{a,e}, Ralph Leijenaar^{a,e}, Sara Carvalho^{a,e}, Ruud G.P.M. van Stiphout^{a,e}, Patrick Granton^{a,e}, Catharina M.L. Zegers^{a,e}, Robert Gillies^{b,e}, Ronald Boellard^{c,e}, André Dekker^{a,e}, and Hugo J.W.L. Aerts^{a,d,e}

^aDepartment of Radiation Oncology (MAASTRO), GROW – School for Oncology and Developmental Biology, Maastricht University Medical Center, Maastricht, The Netherlands ^bH. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA ^cU University Medical Center, Department of Nuclear Medicine & PET Research, Amsterdam, The Netherlands ^dComputational Biology and Functional Genomics Laboratory, Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Harvard School of Public Health, USA

Comprehensive quantification of disease phenotypes by applying a large number of quantitative image features representing lesion heterogeneity and correlating with clinical data and omics



PET radiomics characterize breast cancer subtypes

54 patients with breast cancer prior biopsy

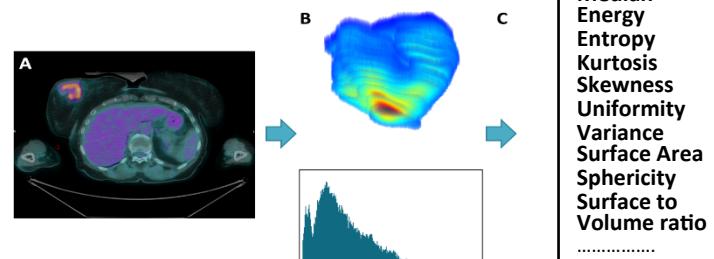
Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-017-3770-9



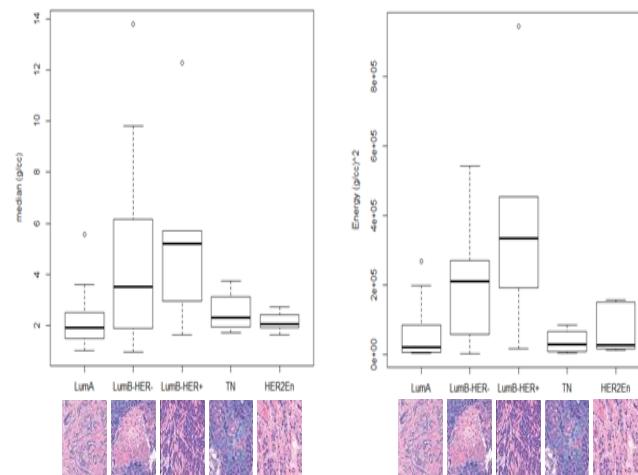
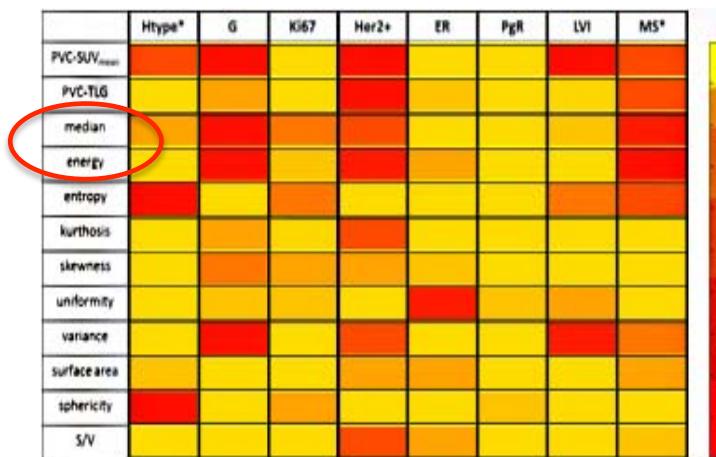
ORIGINAL ARTICLE

[¹⁸F]FDG PET/CT features for the molecular characterization of primary breast tumors

Lidija Antunovic¹ · Francesca Gallivanone² · Martina Sollini³ · Andrea Sagona⁴ · Alessandra Invento⁵ · Giulia Manfrinato⁶ · Margarita Kirienko³ · Corrado Tinterri⁴ · Arturo Chiti^{1,3} · Isabella Castiglioni²



PET radiomic features vs himmunochemistry molecular factors and molecular subtypes (5)*



Statistical correlations with omics

MRI-DWI radiomics characterize breast cancer response

38 Breast cancer patients treated with NAC + surgery

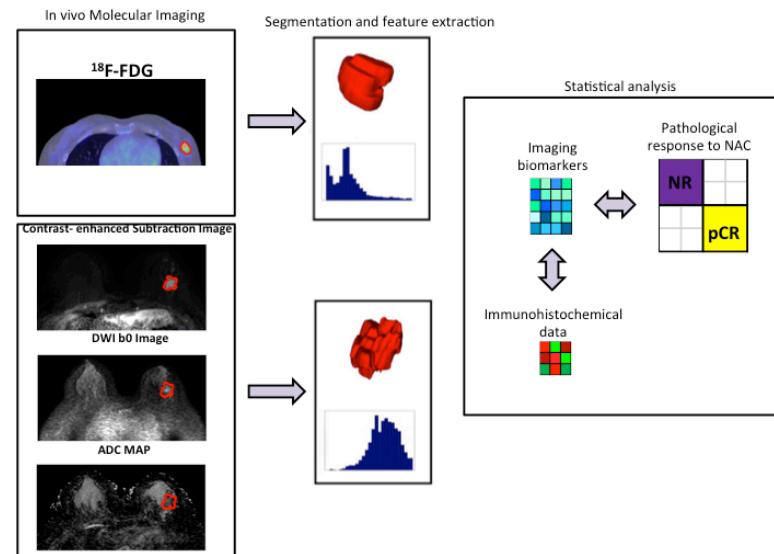
Magn Reson Mater Phy (2017) 30:359–373
DOI 10.1007/s10334-017-0610-7



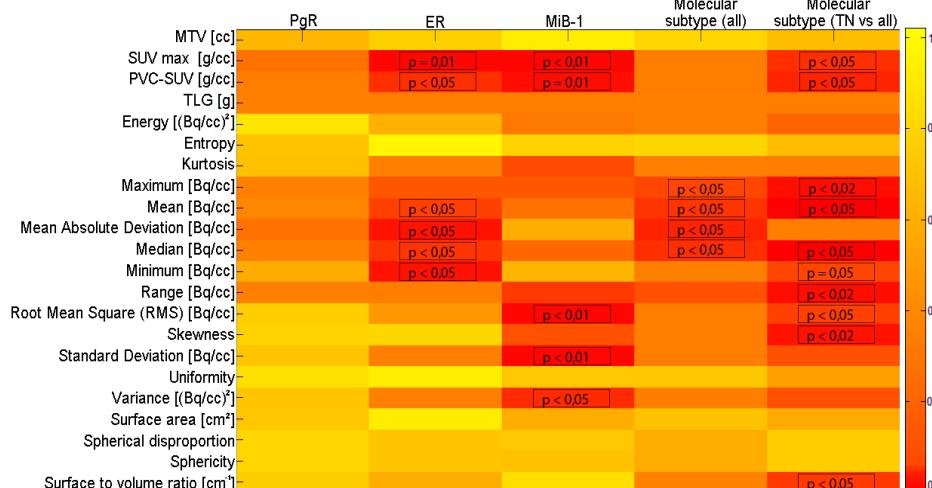
RESEARCH ARTICLE

Biomarkers from in vivo molecular imaging of breast cancer: pretreatment ^{18}F -FDG PET predicts patient prognosis, and pretreatment DWI-MR predicts response to neoadjuvant chemotherapy

Francesca Gallivanone¹ · Marta Maria Panzeri² · Carla Canevari³ · Claudio Losio² · Luigi Gianolli³ · Francesco De Cobelli^{2,4} · Isabella Castiglioni¹

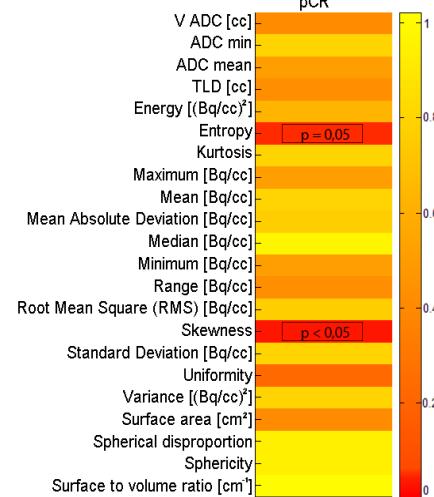


PET radiomic features vs himmunochemistry molecular factors



Statistical correlations with omics

MRI-DWI radiomic features VS NAC pCR



Statistical correlations with clinical data

PET radiomics characterize NSCL response to treatment

[Frontiers in Bioscience, Landmark, 22, 1713-1723, June 1, 2017]

FDG PET/CT as theranostic imaging in diagnosis of non-small cell lung cancer

Margarita Kirienko¹, Francesca Gallivanone², Martina Sollini¹, Giulia Veronesi³, Emanuele Voulaz³, Lidija Antunovic⁴, Lorenzo Leonardi⁴, Giorgio Testanera⁴, Isabella Castiglioni², Arturo Chiti^{1,4}

¹Department of Biomedical Sciences, Humanitas University, Rozzano, Milan, Italy, ²IBFM-CNR, Segrate, Milan, Italy, ³Thoracic Surgery, Humanitas Clinical and Research Center, Rozzano, Milan, Italy, ⁴Nuclear Medicine, Humanitas Clinical and Research Center, Rozzano, Milan, Italy

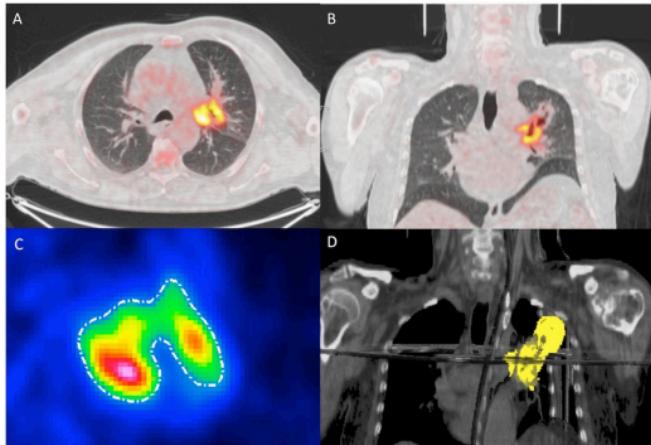
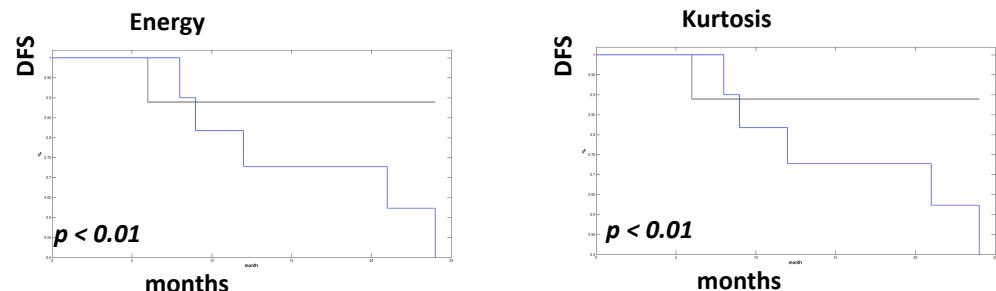


Figure 1. A 67-year-old male with squamous cell carcinoma, G3pT3N1 (stage IIIa) who underwent pneumonectomy and subsequent adjuvant chemotherapy with cisplatin and vinorelbine. After 36 months' follow-up the patient had no evidence of disease. PVC-SUV = 15.59 g/cc, SUVmax = 21.18 g/cc, Energy = 3.2E06 (g/cc)2, Entropy = 4.08, Kurtosis = 3.85. The axial (A) and coronal (B) fused PET/CT images show the lesion in the upper left lobe; the axial PET (C) image shows the tumour segmentation operated by the algorithm; (D) metabolic tumour volume visualized on CT images.

30 Non-Small Cell lung cancer patients treated with surgery + NAC

Survival endpoint	PET feature	P-value	Cut-off	Sensitivity	Specificity
DSF	Energy[(MBq/cc) ²]	0.01	2.74	87.5%	75%
	Kurtosis	<0.05	2.71	75%	60%
DMFS	PVC-SUV _{mean}	<0.05	11.91	80%	80%
	SUV _{max}	<0.05	14.84	80%	80%
Energy[(MBq/cc) ²]	Energy[(MBq/cc) ²]	<0.05	2.74	100%	80%
	Kurtosis	<0.05	2.9	100%	75%



Statistical correlations with clinical data

Predictive personalized medicine by radiomics

www.nature.com/scientificreports/

SCIENTIFIC REPORTS

OPEN

Machine Learning methods for Quantitative Radiomic Biomarkers

Chintan Parmar^{1,3,4,*}, Patrick Grossmann^{1,5,*}, Johan Bussink⁶, Philippe Lambin³ & Hugo J. W. L. Aerts^{1,2,5}

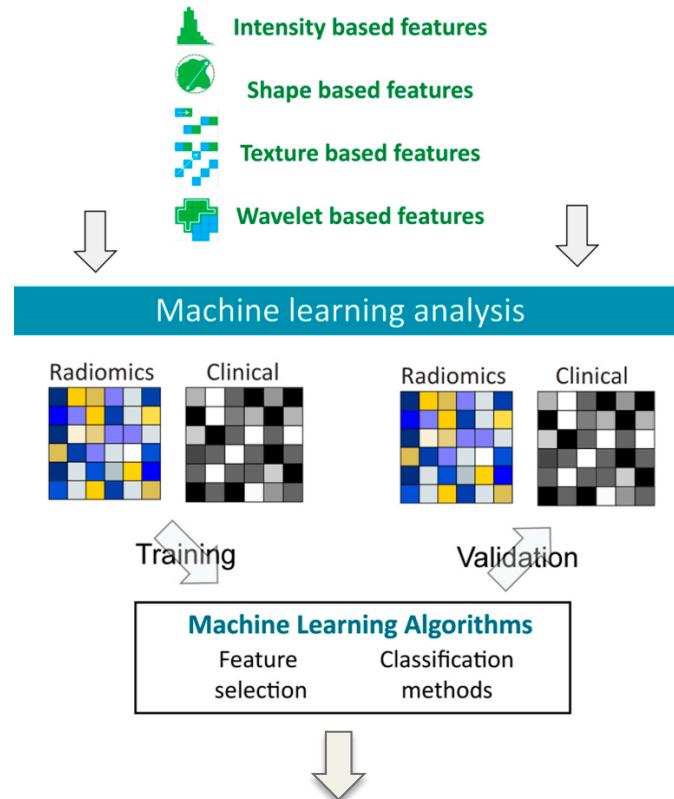
Received: 02 April 2015

Accepted: 17 August 2015

Published: 27 August 2015

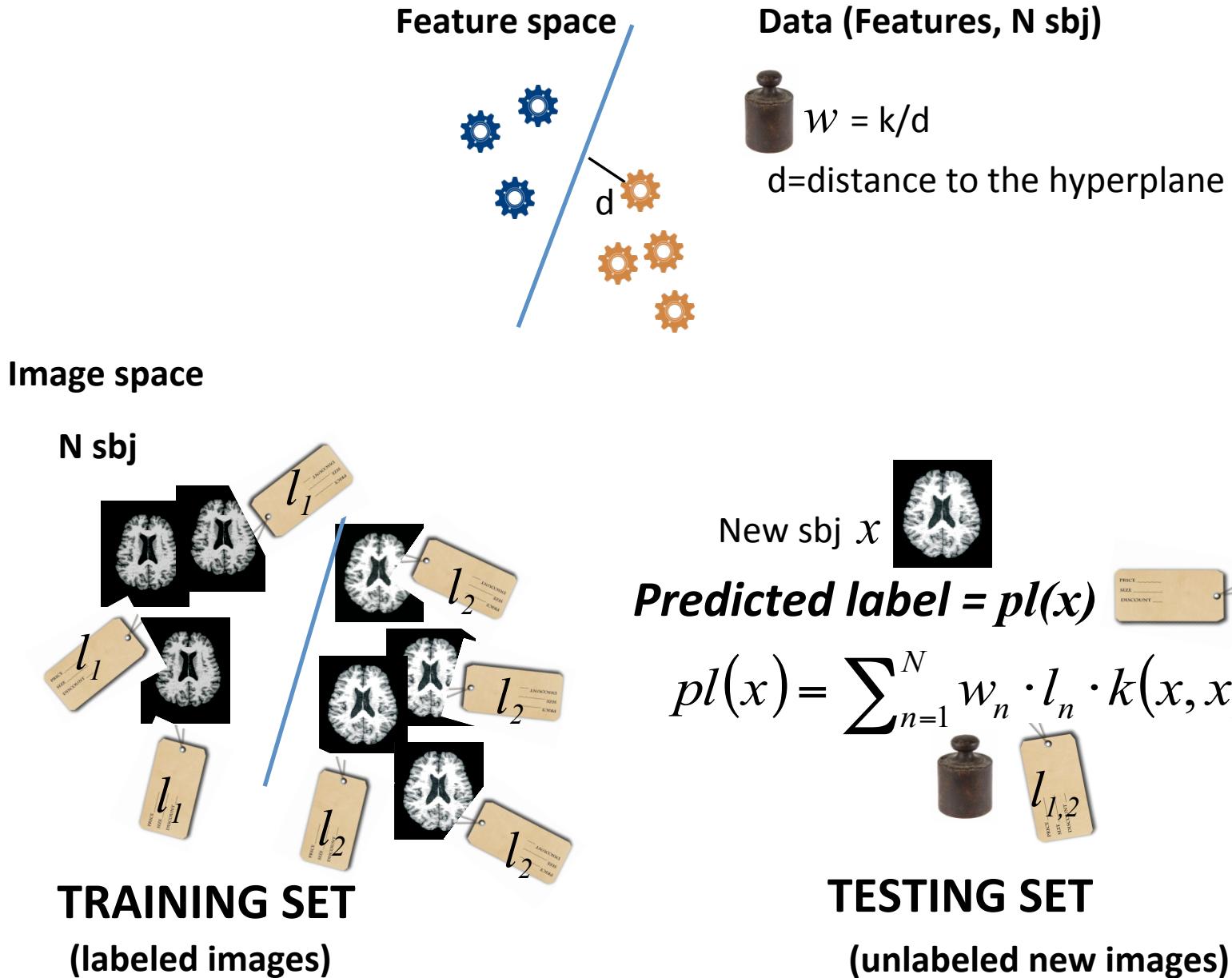
Radiomics extracts and mines large number of medical imaging features quantifying tumor phenotypic characteristics. Highly accurate and reliable machine-learning approaches can drive the

To predict clinical outcome by applying artificial intelligence models to radiomics features



Predictive models based on Radiomics features

The Predictive Model



MRI & AI for PD brain studies



Contents lists available at ScienceDirect

Journal of Neuroscience Methods

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



Clinical Neuroscience

Machine learning on brain MRI data for differential diagnosis of Parkinson's disease and Progressive Supranuclear Palsy

C. Salvatore^a, A. Cerasa^b, I. Castiglioni^{c,*}, F. Gallivanone^c, A. Augimeri^b, M. Lopez^d, G. Arabia^e, M. Morelli^e, M.C. Gilardi^c, A. Quattrone^{b,e}

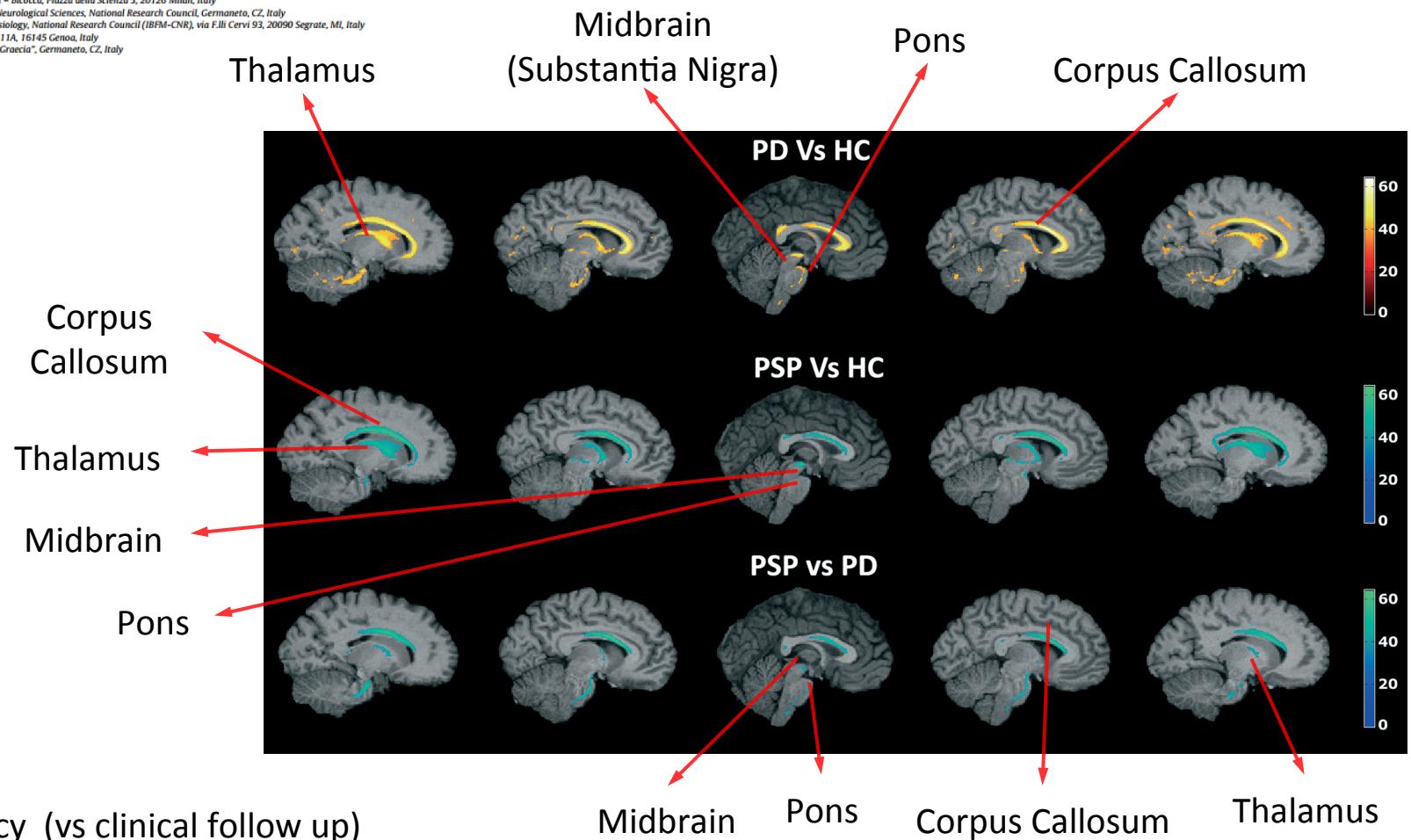
^a Department of Physics, University of Milan – Bicocca, Piazza della Scienza 3, 20126 Milan, Italy

^b Neuroimaging Research Unit, Institute of Neurological Sciences, National Research Council, Germaneto, CZ, Italy

^c Institute of Molecular Bioimaging and Physiology, National Research Council (IBFM-CNR), via F.lli Cervi 93, 20090 Segrate, MI, Italy

^d DITEN, University of Genoa, Via Opera Pia 11A, 16145 Genoa, Italy

^e Institute of Neurology, University "Magna Graecia", Germaneto, CZ, Italy



MRI & AI for AD brain studies



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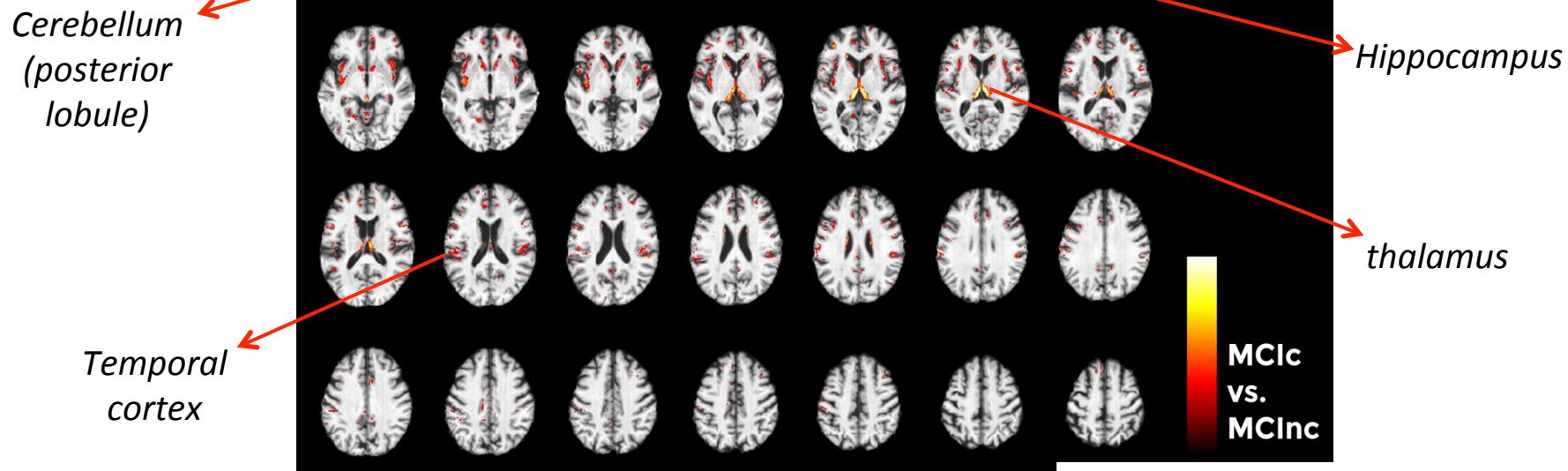
Edited by:
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Della Caffarra, University of Miami, USA
Li-Wen Kuo,
National Health Research Institute, Taiwan
Correspondence:
Isabella Castiglioni,
Institute of Molecular Biomedicine and
Physiology, National Research Council

Magnetic resonance imaging biomarkers for the early diagnosis of Alzheimer's disease: a machine learning approach

Christian Salvatore¹, Antonio Cerasa², Petronilla Battista¹, Maria C. Gilardi¹,
Aldo Quattrone¹, Isabella Castiglioni^{1,2*} and
the Alzheimer's Disease Neuroimaging Initiative¹

¹Neurology Department, National Research Council (INFM-CNR), Milan, Italy; ²Neuroimaging Research Unit, Institute of Molecular Biomedicine and Physiology, National Research Council (INFM-CNR), Catanzaro, Italy;

*Department of Medical Sciences, Institute of Neurology, University "Magna Graecia", Catanzaro, Italy.



85% Accuracy (vs clinical follow up)

MRI Characterizes the Progressive Course of AD and Predicts Conversion to Alzheimer's Dementia 24 Months Before Probable Diagnosis

Christian Salvatore¹, Antonio Cerasa² and Isabella Castiglioni^{1,2*}
the Alzheimer's Disease Neuroimaging Initiative¹

Frontiers in Aging Neuroscience | www.frontiersin.org | Volume 10 | Article 135 | April 2018 | doi:10.3389/fnagi.2018.00135

Advantages for brain studies

- Validated segmentation methods (Grey matter, White matter, CSF)
- Images can be co-registered
- Large database of images exists (ADNI, PPMI, AIBL, CLSA...)

Problems for oncological studies

- Lesions (small, heterogeneus, irregular shape)
- Segmentation methods are not validated for heterogeneus and non-spherical lesions
- Images cannot be co-registered (results can be imaged for single-subject)
- Large database of images do not exist

Solutions

- Automatic segmentation of lesion volume on PET images

978-1-4799-0534-8/13/\$31.00 ©2013 IEEE

Adaptive threshold method based on PET measured
lesion-to-background ratio for the estimation of
Metabolic Target Volume from ^{18}F -FDG PET images

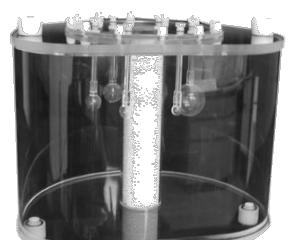
Francesca Gallivanone, Federico Fazio, Luca Presotto, *Member, IEEE*, Maria C. Gilardi, Carla Canevari, Isabella Castiglioni

Hindawi Publishing Corporation
Computational and Mathematical Methods in Medicine
Volume 2015, Article ID 571473, 12 pages
<http://dx.doi.org/10.1155/2015/571473>

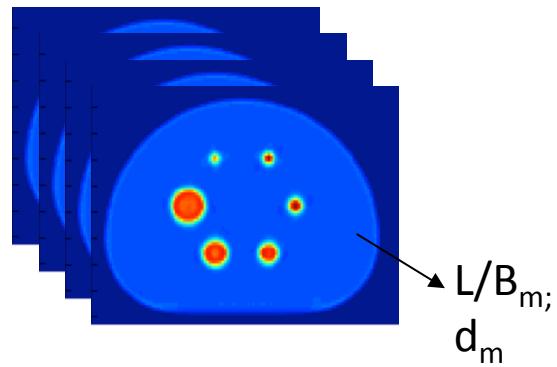
Research Article

**An Adaptive Thresholding Method for BTV
Estimation Incorporating PET Reconstruction Parameters:
A Multicenter Study of the Robustness and the Reliability**

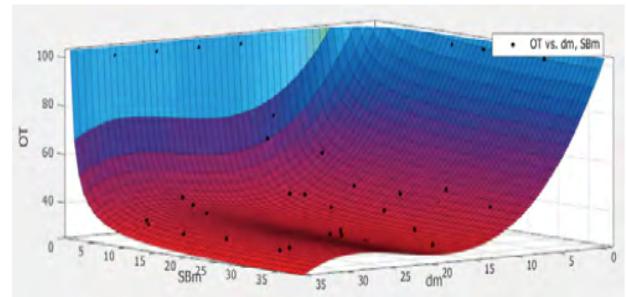
M. Brambilla,¹ R. Matheoud,¹ C. Basile,² C. Bracco,³ I. Castiglioni,⁴ C. Cavedon,⁵
M. Cremonesi,⁶ S. Morzenti,⁷ F. Fioroni,⁸ M. Giri,⁵ F. Botta,⁶ F. Gallivanone,⁴
E. Grassi,⁸ M. Pacilio,² E. De Ponti,⁷ M. Stasi,³ S. Pasetto,⁹ S. Valzano,¹ and D. Zanni⁹



NEMA IQ phantom



Adaptative Threshold = function of L/B_m and d_m



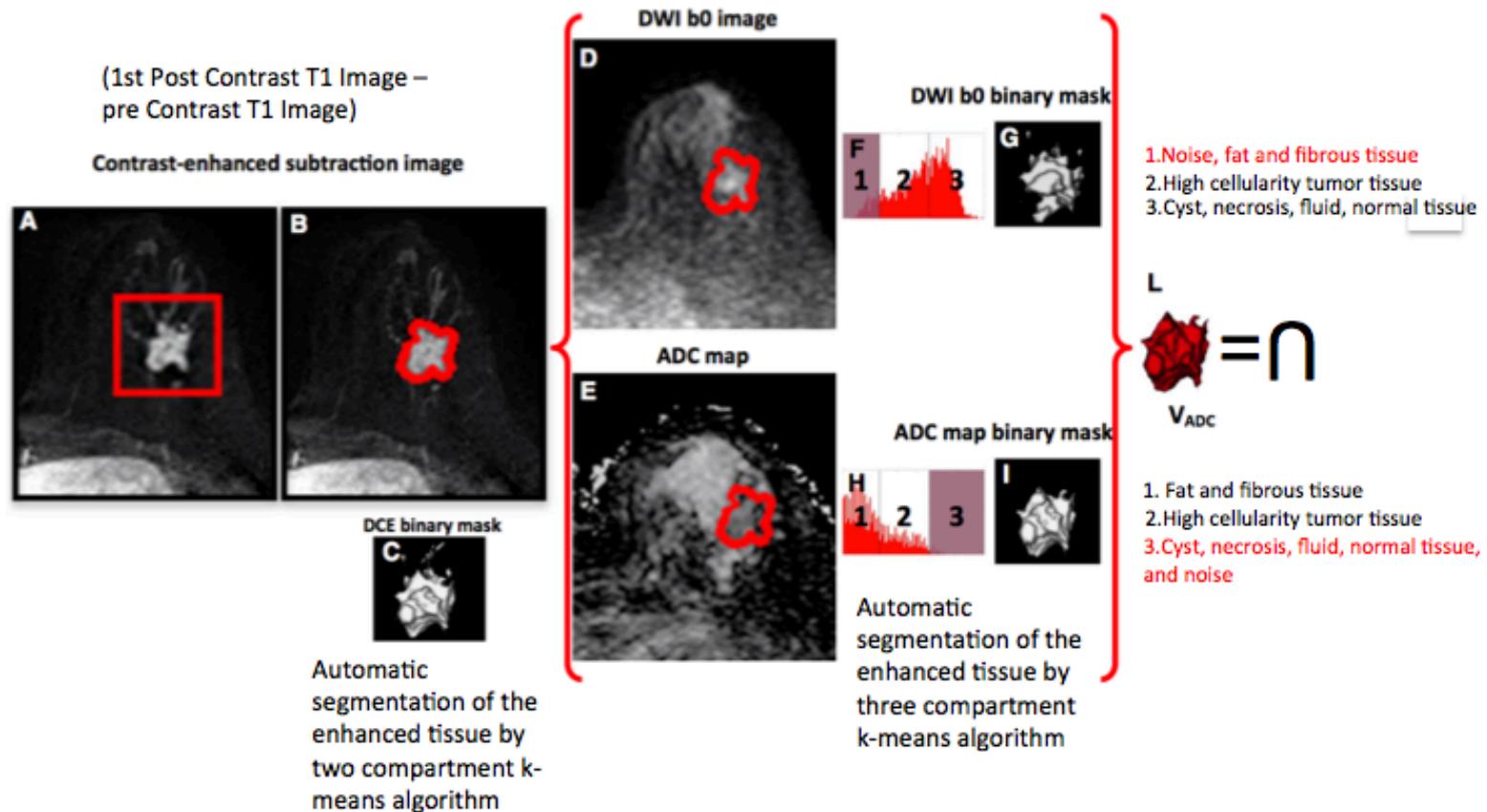
Solutions

- Automatic segmentation of lesion volume on MRI images

An Automatic Segmentation Method for the Measurement of the Functional Volume of Oncological Lesions on MR ADC Maps

Francesca Gallivanone, Marta Maria Panzeri, Carla Canevari, Interlenghi Matteo, Claudio Losio, Luca Gianolli, Francesco De Cobelli, and Castiglioni Isabella

978-1-5090-1642-6/16/\$31.00 ©2016 IEEE



Validation on small, heterogeneous, non-spherical lesions

Jinst

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INTERNATIONAL WORKSHOP ON IMAGING
7–10 SEPTEMBER 2015
VARENNA, ITALY

A fully automatic, threshold-based segmentation method for the estimation of the Metabolic Tumor Volume from PET images: validation on 3D printed anthropomorphic oncological lesions

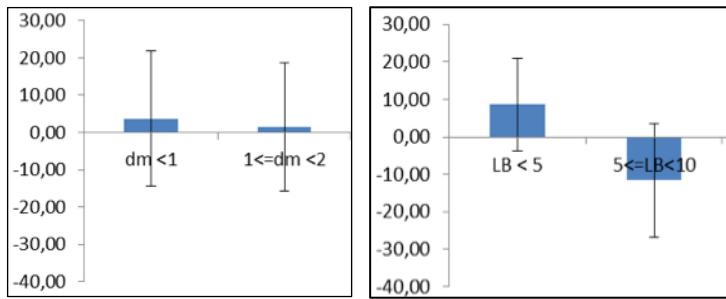
F. Galivani^a, M. Interviglio^b, C. Cenervi^b and I. Castiglioni^{a,1}

^aInstitute of Molecular Imaging and Physiology, National Research Council, Trieste, Italy

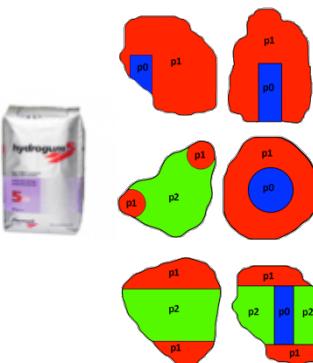
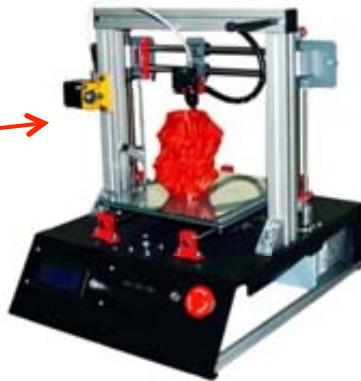
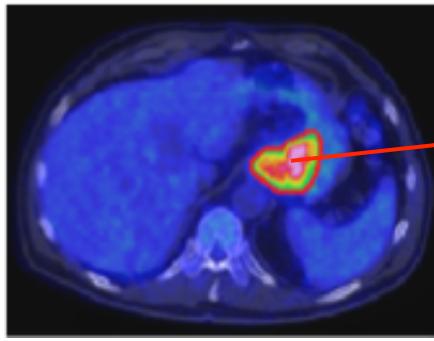
^bDivision of Nuclear Medicine, IRCCS San Raffaele Scientific Institute, via Olgettina 60, 20132 Milan, Italy

E-mail: isabella.castiglioni@ibfm.cnr.it

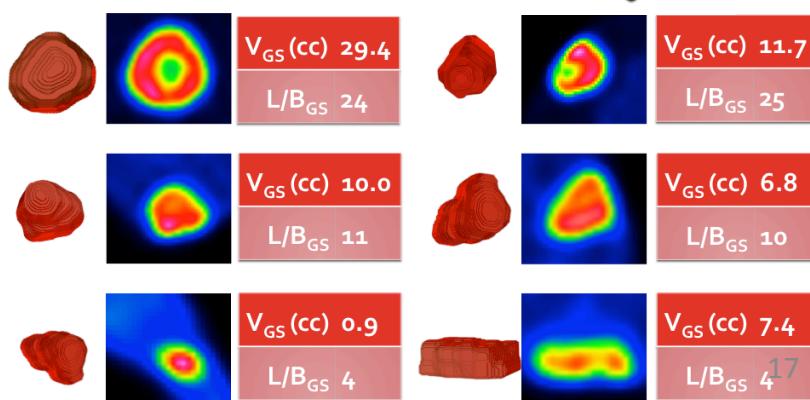
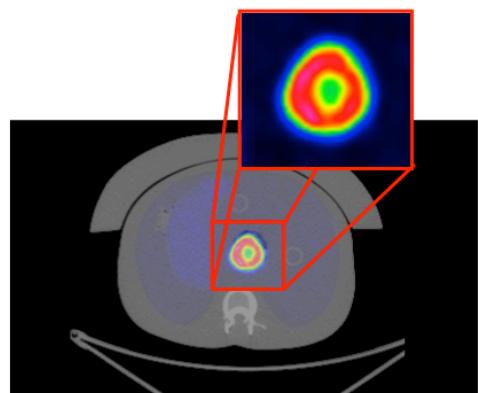
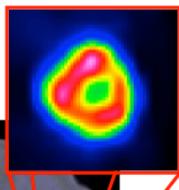
% residual error in V_m



d (mm)	% residual error after PVE correction
9.8	0.26±0.12
12.3	0.13±0.06
15.6	0.002±0.002
25.8	0.09±0.03
31.3	0.10±0.01



Selected as highlight at IEEE NSS MIC, Strasburgh, November 2016



Real patient

Anthropomorphic phantom with syntethic lesion

Radiomics: what is the state of the art?

Clinical and Translational Imaging (2018) 6:411–413
<https://doi.org/10.1007/s40336-018-0302-y>

SPOTLIGHT

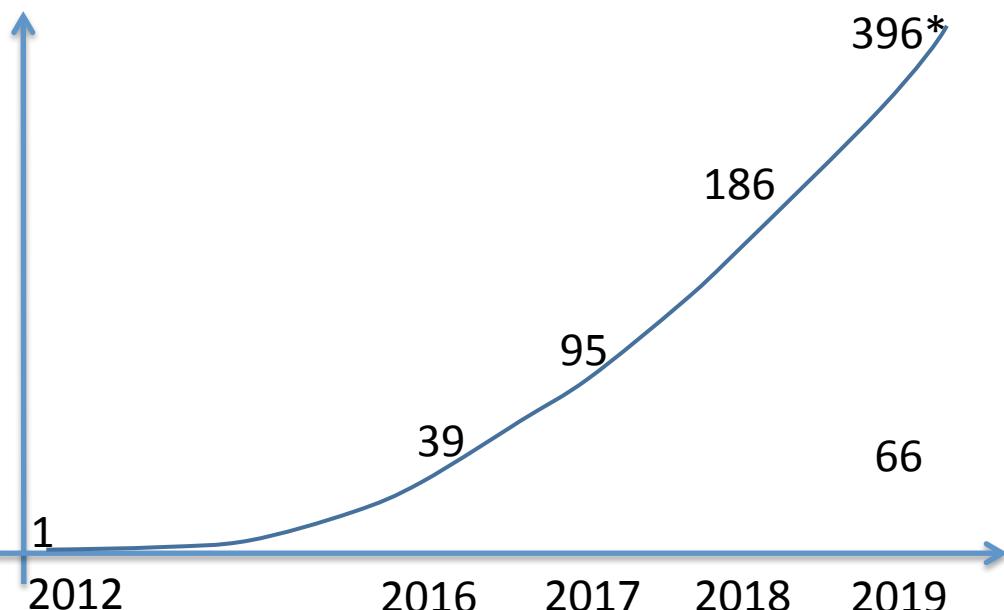


Radiomics: is it time to compose the puzzle?

Isabella Castiglioni¹ · Maria Carla Gilardi¹

Received: 29 September 2018 / Accepted: 3 October 2018 / Published online: 15 October 2018
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Hindawi
Contrast Media & Molecular Imaging
Volume 2019, Article ID 7919545, 2 pages
<https://doi.org/10.1155/2019/7919545>



Editorial Frontiers from Radiomics in Molecular Imaging

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A study in which we hope to never be cited....



PLOS ONE | DOI:10.1371/journal.pone.0124165 May 4, 2015

RESEARCH ARTICLE

False Discovery Rates in PET and CT Studies with Texture Features: A Systematic Review

Anastasia Chalkidou*, Michael J. O'Doherty, Paul K. Marsden

Division of Imaging Sciences and Biomedical Engineering, Kings College London 4th Floor, Lambeth Wing, St. Thomas Hospital, SE1 7EH, London, United Kingdom

* anastasia.chalkidou@kcl.ac.uk

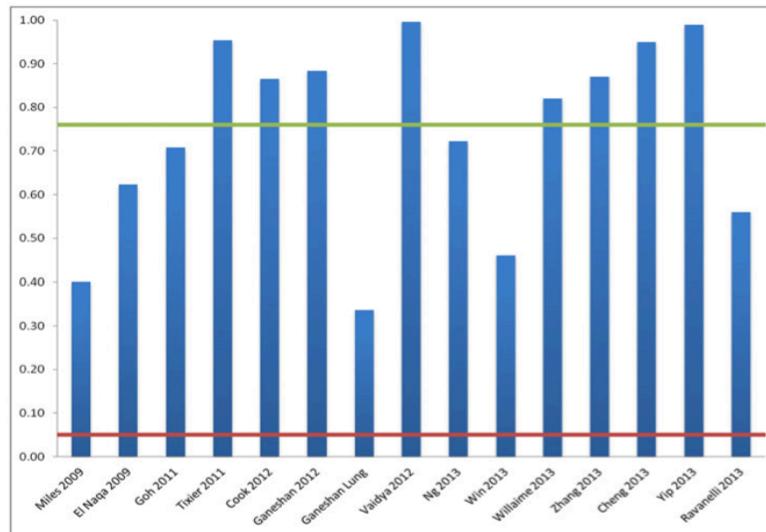


Fig 2. Probability of a false positive result based on number of hypotheses tested per study (blue columns) for all study categories. 5% type-I error probability = red line, average type-I error probability (76%) over all studies = green line (Note—additional inflation of the type-I error probability due to the use of the optimum cut-off approach is not included here).

Biological change or radiomic instability?

- Repeatability
- Reproducibility
- Significance

Stability

- There is currently no consensus on the tolerated variability of radiomics features for the evaluation of prognosis or response to treatment.

Radiomic Repeatability/Reproducibility/Significance

Hindawi
Contrast Media & Molecular Imaging
Volume 2018, Article ID 5324517, 12 pages
<https://doi.org/10.1155/2018/5324517>

Research Article

Parameters Influencing PET Imaging Features: A Phantom Study with Irregular and Heterogeneous Synthetic Lesions

Francesca Gallivanone,¹ Matteo Interlenghi,¹ Daniela D'Ambrosio,²
Giuseppe Trifirò,³ and Isabella Castiglioni¹

¹Institute of Molecular Bioimaging and Physiology, National Research Council (IBFM-CNR), Milan, Italy

²Medical Physics Unit, IRCCS Fondazione S. Maugeri, Pavia, Italy

³Nuclear Medicine Unit, IRCCS Fondazione S. Maugeri, Pavia, Italy



Repeatability

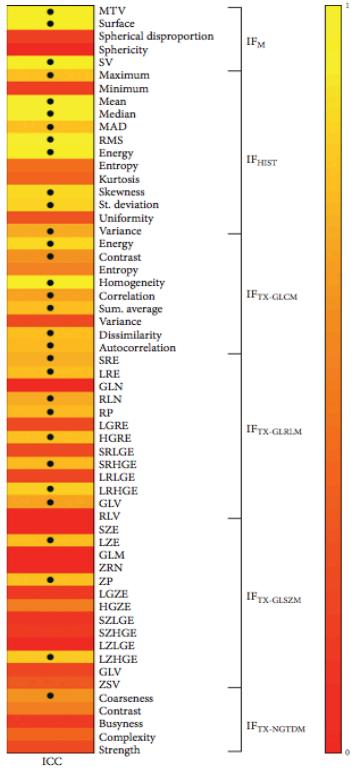


FIGURE 6: Reproducibility of radiomic features on test-retest datasets. ICC results. • indicates $\text{ICC} \geq 0.6$.

Reproducibility

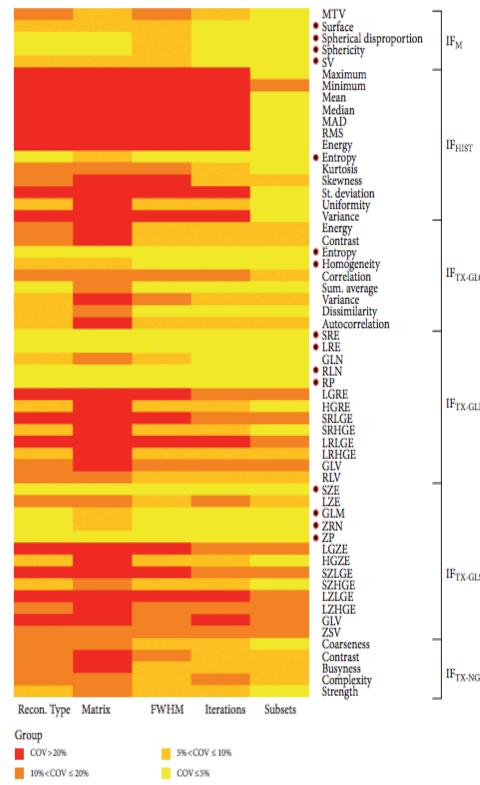


FIGURE 5: Stability of radiomic features on different reconstruction settings. COV results. • indicates $\text{COV} \leq 10\%$

Significance

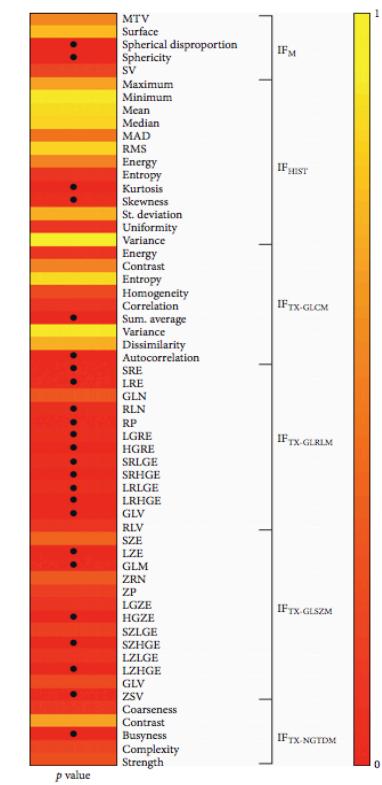


FIGURE 7: Mann-Whitney test results (p value). • indicates p value < 0.05 .

A possible solution?



A post-reconstruction harmonization method for multicenter radiomic studies in PET

Fanny Orlhac, Sarah Boughdad, Cathy Philippe, Hugo Stalla-Bourdillon, Christophe Nioche, Laurence Champion, Michaël Soussan, Frédérique Frouin, Vincent Frouin and Irène Buvat

J Nucl Med.
Published online: January 4, 2018.
Doi: 10.2967/jnumed.117.199935

Harmonization method

To pool SUV and textural features measured from different PET protocols, we tested a harmonization method previously described for genomic studies to correct the so-called batch effect. The ComBat harmonization model developed by Johnson et al (25) assumes that the value of each feature y measured in VOI j and scanner i can be written as:

$$y_{ij} = \alpha + X_{ij}\beta + \gamma_i + \delta_i \varepsilon_{ij} \quad \text{Equation 1}$$

where α is the average value for feature y , X is a design matrix for the covariates of interest, β is the vector of regression coefficients corresponding to each covariate, γ_i is the additive effect of scanner i on features supposed to follow a normal distribution, δ_i describes the multiplicative scanner effect supposed to follow an inverse gamma distribution, and ε_{ij} is an error term (normally distributed with a zero mean), as explained in Fortin et al (30). ComBat harmonization consists in estimating γ_i and δ_i using Empirical Bayes estimates (noted γ_i^* and δ_i^*) as described in (25). The normalized value of feature y for VOI j and scanner i is then obtained as:

$$y_{ij}^{\text{ComBat}} = \frac{y_{ij} - \hat{\alpha} - X_{ij}\hat{\beta} - \gamma_i^*}{\delta_i^*} + \hat{\alpha} + X_{ij}\hat{\beta} \quad \text{Equation 2}$$

where $\hat{\alpha}$ and $\hat{\beta}$ are estimators of parameters α and β respectively. The ComBat harmonization determines a transformation for each feature separately based on the batch (here Department) effect observed on feature values. In the first part of this study, we used ComBat without accounting for any biological covariate (ie $X=0$), and, in the second part, we used the TN status as the covariate of interest.

For each tissue separately (tumor and liver tissues), we applied ComBat harmonization on all features using the R function called “combat” available at <https://github.com/Jfortin1/ComBatHarmonization/>.

Results

“centre effect” on 9 PET radiomic features from breast cancer patients (63 A vs 74 B)

					After ComBat			
	TN(A) vs TN(B)	non-TN(A) vs non-TN(B)	TN(A+B) vs TN(B) vs non-TN(A+B)	TN(A) vs TN(A)	TN(A) vs TN(B)	non-TN(A) vs non-TN(B)	TN(A+B) vs non-TN(A+B)	TN(B) vs non-TN(A)
Homogeneity	0.4232	0.0074	0.0014	0.4635	0.5986	0.8737	0.0015	0.0093
Entropy	0.5196	0.3906	0.0031	0.0875	0.7405	0.9139	0.0027	0.0254
SRE	0.2995	0.00044	0.0063	0.9481	0.1294	0.8338	0.0062	0.0061
LRE	0.2814	0.0004	0.0072	0.9352	0.0055	0.3871	0.0162	0.0004
LGZE	0.0405	0.0244	5.69e-05	0.3786	0.1102	0.3059	0.0002	0.0003
HGZE	0.0494	0.0282	3.20e-05	0.2886	0.2814	0.3337	2.27e-05	0.0058
SUVmax	0.0544	0.0278	7.54e-05	0.4058	0.5717	0.7943	4.47e-05	0.0072
SUVmean	0.0448	0.0359	3.20e-05	0.2394	0.4463	0.7747	3.05e-05	0.0052
SUVpeak	0.0267	0.0306	9.75e-05	0.4736	0.3581	0.7894	4.99e-05	0.0061

Table 3: P-values of Wilcoxon’s test for all features between TN and non-TN lesions from Departments A and B, before and after ComBat harmonization. Bold values are less than 0.05.

A recommendation....

**Test radiomic results on
different and independent image data sets!**

Radiomics: a new approach for the study of cancer



HHS Public Access

Author manuscript

Eur J Cancer. Author manuscript; available in PMC 2015 August 12.

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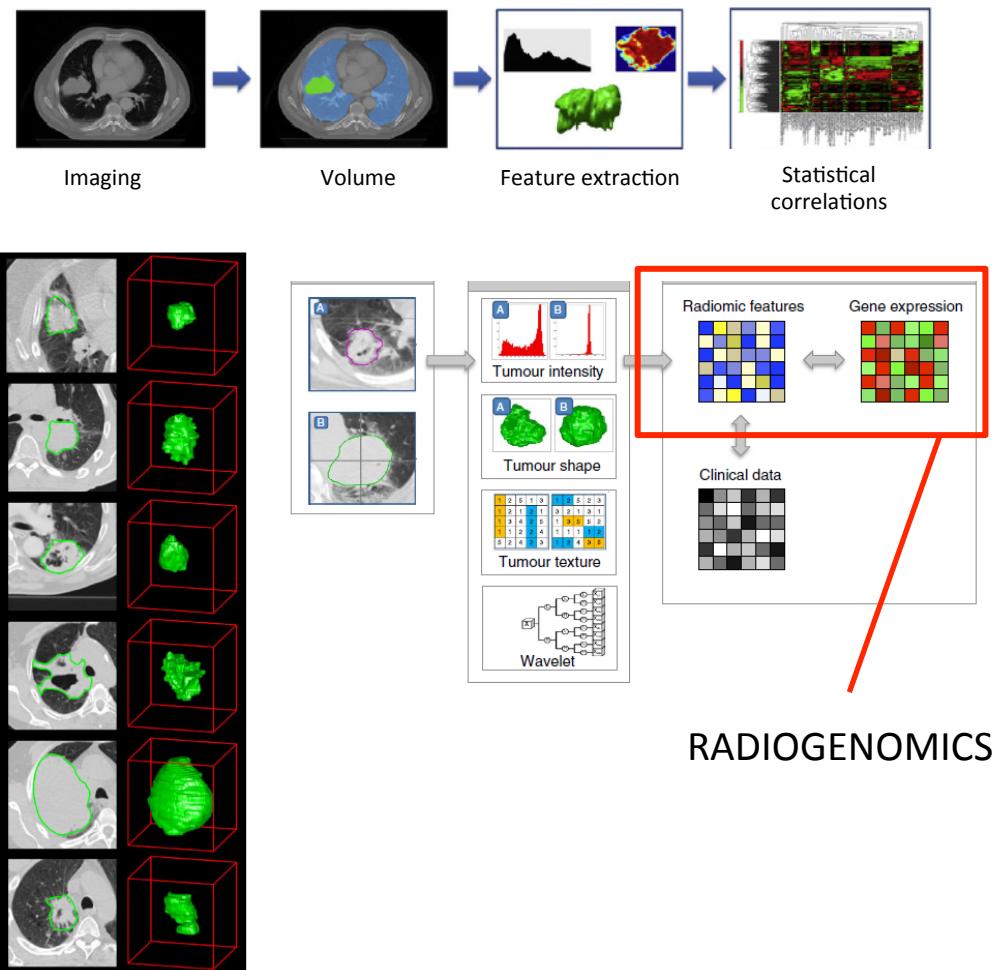
Eur J Cancer. 2012 March ; 48(4): 441–446. doi:10.1016/j.ejca.2011.11.036.

Radiomics: Extracting more information from medical images using advanced feature analysis

Philippe Lambin^{a,*}, Emmanuel Rios-Velazquez^{a,e}, Ralph Leijenaar^{a,e}, Sara Carvalho^{a,e}, Ruud G.P.M. van Stiphout^{a,e}, Patrick Granton^{a,e}, Catharina M.L. Zegers^{a,e}, Robert Gillies^{b,e}, Ronald Boellard^{c,e}, André Dekker^{a,e}, and Hugo J.W.L. Aerts^{a,d,e}

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Comprehensive quantification of disease phenotypes by applying a large number of quantitative image features representing lesion heterogeneity and correlating with clinical data and omics



CT radiogenomics for cancer

Non-Small Cell Lung Cancer: Identifying Prognostic Imaging Biomarkers by Leveraging Public Gene Expression Microarray Data— Methods and Preliminary Results¹

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Jiajing Xu, MS
Chuong D. Hoang, MD
Ann N. Leung, MD
Yue Xu, PhD
Andrew Quon, MD
Daniel L. Rubin, MD, MS
Sandy Napel, PhD
Sylvia K. Plevritis, PhD

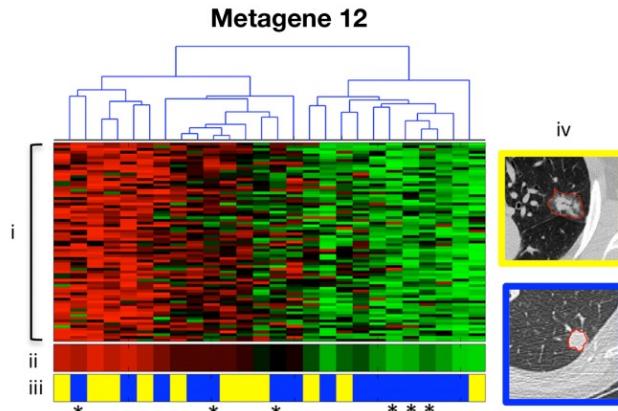
Purpose:

To identify prognostic imaging biomarkers in non-small cell lung cancer (NSCLC) by means of a radiogenomics strategy that integrates gene expression and medical images in patients for whom survival outcomes are not available by leveraging survival data in public gene expression data sets.

Materials and Methods:

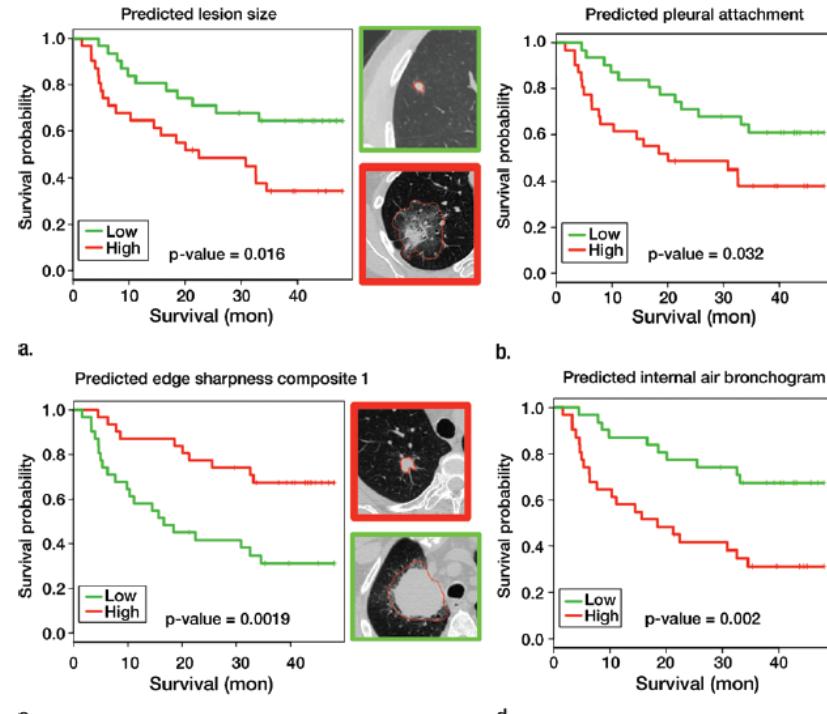
A radiogenomics strategy for associating image features with clusters of coexpressed genes (metagenes) was defined. First, a radiogenomics correlation map is created

Radiology: Volume 264: Number 2 – August 2012 • radiology.rsna.org



Non-Small Cell lung cancer

4 CT image features



Our approach to radiogenomics: subtypes from system medicine

Published online 23 December 2015

Nucleic Acids Research, 2016, Vol. 44, No. 8 e71
doi: 10.1093/nar/gkv1507

TCGAbiolinks: an R/Bioconductor package for integrative analysis of TCGA data

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Theranostics 2015, Vol. 5, Issue 10

1122



Theranostics

2015; 5(10): 1122-1143. doi: 10.7150/thno.11543

Review

MicroRNAs: New Biomarkers for Diagnosis, Prognosis, Therapy Prediction and Therapeutic Tools for Breast Cancer

Gloria Bertoli, Claudia Cava, and Isabella Castiglioni^{1,2}

Institute of Molecular Bioimaging and Physiology (IBFM), National Research Council (CNR), Milan, Italy.

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Received: 2015.01.09; Accepted: 2015.06.17; Published: 2015.07.13



Article

SpidermiR: An R/Bioconductor Package for Integrative Analysis with miRNA Data

Claudia Cava ^{1,*}, Antonio Colaprico ^{2,3}, Gloria Bertoli ¹, Alex Graudenzi ¹, Tiago C. Silva ⁴, Catharina Olsen ^{2,3}, Houtan Noushmehr ^{4,5}, Gianluca Bontempi ^{2,3}, Giancarlo Mauri ^{6,7} and Isabella Castiglioni ^{1,*}

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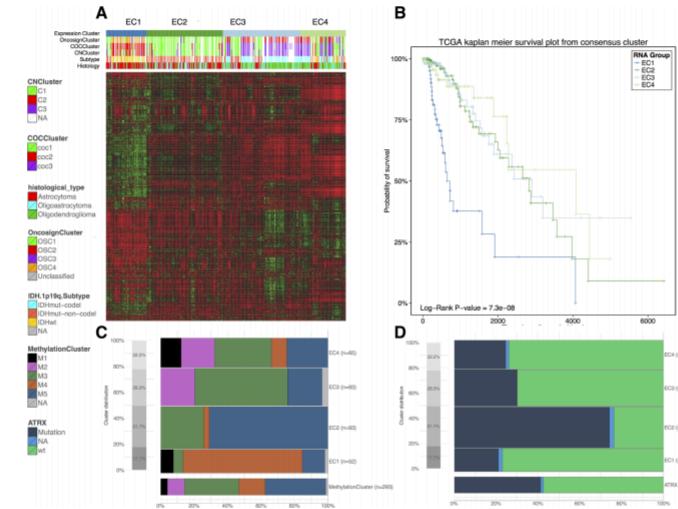
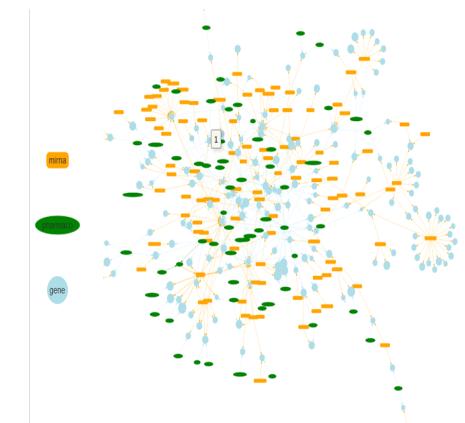


Figure 4. Case study 2 Integrative (or Downstream) analysis of gene expression and clinical data from LGG disease with unsupervised clustering and crossing expression clusters with clinical and molecular information. (A) Heatmap of 1187 more variables genes clustered with tree $k = 4$ in EC1, EC2, EC3, EC4. (B) Kaplan Meier survival plot for EC clusters. (C and D) Distribution of the DNA Methylation clusters and ATRX mutation within the EC clusters.



Breast cancer system biology

The Author(s) BMC Bioinformatics 2016, 17(Suppl 12):348
DOI 10.1186/s12859-016-1196-1

BMC Bioinformatics

RESEARCH

Open Access



How interacting pathways are regulated by miRNAs in breast cancer subtypes

Claudia Cava¹, Antonio Colaprico^{2,3}, Gloria Bertoli¹, Gianluca Bontempi^{2,3}, Giancarlo Mauri⁴ and Isabella Castiglioni^{1*}

From Twelfth Annual Meeting of the Italian Society of Bioinformatics (BITS)
Milan, Italy, 3-5 June 2015

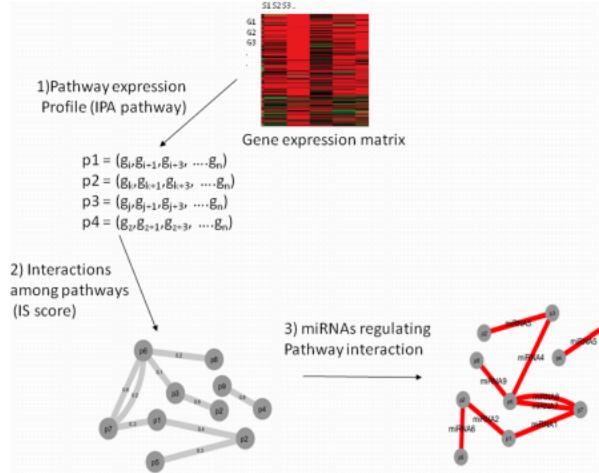


Table 1. Unique pathways enriched of differentially expressed genes for each breast cancer subtype: 17 pathways for luminal A, 5 for luminal B, 19 for basal and 16 for HER2

LUMINAL A	LUMINAL B	BASAL	HER2
REACTOME degradation of the extracellular matrix	KEGG arrhythmogenic right ventricular cardiomyopathy arvc	REACTOME mma splicing	REACTOME activation of the mrna upon binding of the cap binding complex and eifs and subsequent binding to 43s
BIOCARTA intrinsic pathway	REACTOME crmps in sema3a signaling	REACTOME activation of the pre replicative complex	REACTOME unfolded protein response
REACTOME abc family proteins mediated transport	BIOCARTA cellcycle pathway	KEGG spliceosome	REACTOME developmental biology
REACTOME ethanol oxidation	KEGG ribosome	KEGG apoptosis	KEGG ether lipid metabolism
BIOCARTA ami pathway	REACTOME cell junction organization	REACTOME activation of atr in response to replication stress	REACTOME axon guidance
REACTOME metabolism of carbohydrates		KEGG dna replication	REACTOME nucleotide like purinergic receptors
REACTOME glycerophospholipid biosynthesis		REACTOME interferon alpha beta signaling	REACTOME cgpmp effects
REACTOME platelet activation signaling and aggregation		BIOCARTA rams pathway	REACTOME fgr ligand binding and activation
KEGG chemokine signaling pathway		KEGG type i diabetes mellitus	REACTOME phospholipase c mediated cascade
BIOCARTA eryth pathway		BIOCARTA g2 pathway	REACTOME glycolysis
BIOCARTA longevity pathway		KEGG bladder cancer	KEGG histidine metabolism
REACTOME triglyceride biosynthesis		REACTOME s phase	KEGG natural killer cell mediated cytotoxicity
REACTOME transmembrane transport of small molecules		REACTOME g1 s transition	REACTOME asparagine n linked glycosylation
BIOCARTA cfr pathway		REACTOME amino acid synthesis and interconversion transamination	REACTOME p2y receptors
REACTOME o linked glycosylation of mucins		REACTOME metabolism of amino acids and derivatives	REACTOME keratan sulfate keratin metabolism
REACTOME transport of glucose and other sugars bile salts and organic acids metal ions and amine compounds		KEGG arginine and proline metabolism	KEGG melanoma
REACTOME factors involved in macrophage development and platelet production		KEGG glycolysis gluconeogenesis	
		BIOCARTA mcm pathway	
		REACTOME extension of telomeres	

[Frontiers in Bioscience, Landmark, 22, 1697-1712, June 1, 2017]

Pathway-based classification of breast cancer subtypes

Alex Graudenzi^{1,2}, Claudia Cava¹, Gloria Bertoli¹, Bastian Fromm³, Kjersti Flatmark^{3,4,5}, Giancarlo Mauri^{2,6}, Isabella Castiglioni¹*

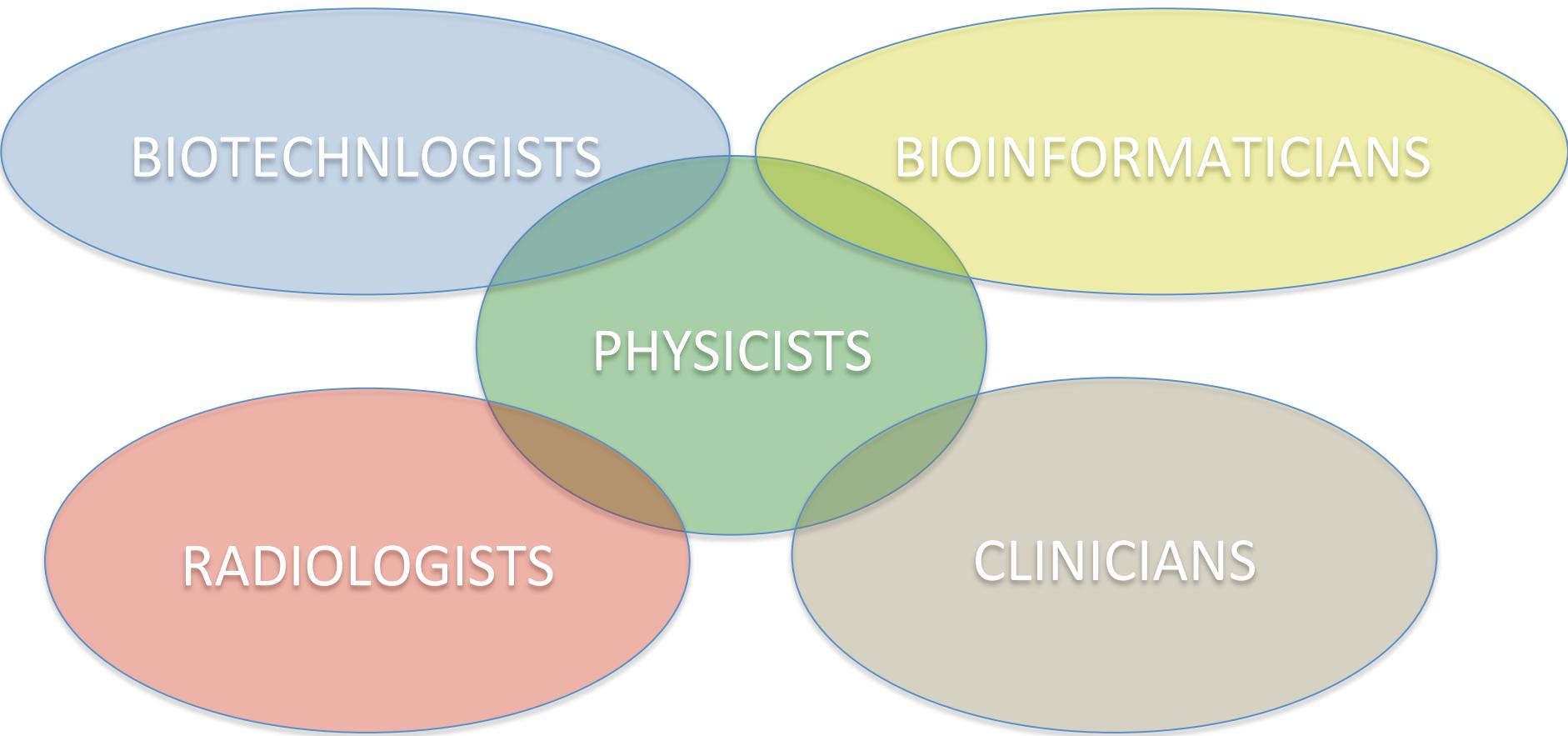
¹Institute of Molecular Bioimaging and Physiology of the Italian National Research Council (IBFM-CNR), Milan, Italy, ²Department of Informatics, Systems and Communication, University of Milan-Bicocca, Milan, Italy, ³Department of Tumor Biology, Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway, ⁴Department of Gastroenterological Surgery, Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway, ⁵Institute of Clinical Medicine, University of Oslo, Oslo, Norway, ⁶SYSBIO Centre of Systems Biology (SYSBIO), 20126 Milan, Italy

Conclusions

- Advanced image processing such as radiomics combined with machine learning can develop models based on imaging signatures for predicting phenotype subtype prognosis and response to therapy
- They are opening new role to in vivo medical imaging in predictive personalized medicine
- Some radiomic methodological issues (e.g. lesion segmentation, feature harmonization and stability) need feasible solutions and validations prior to be translated in clinical studies
- Radiomic predicting models can be improved by epigenomics linked to genomics for integrated phenotype models

How to play the game?

Prospective multi-centre protocols for harmonized radiomic, genomic and clinical data



Competences & Technologies at INLAB[©]

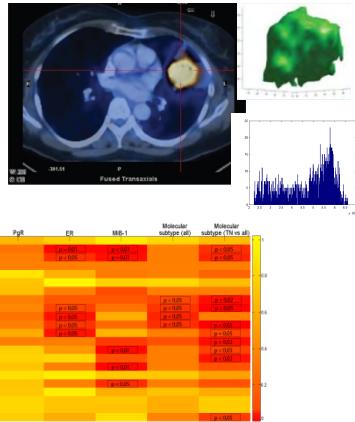


PHYSICIST



Francesca Gallivanone, PhD

PET/MRI/CT
quantitation, SPM, radiomics

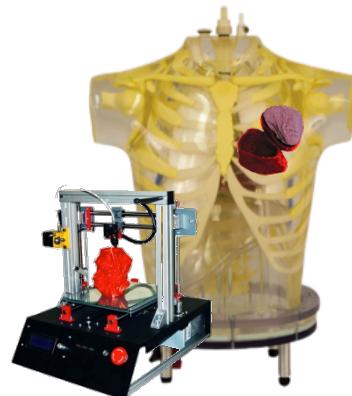


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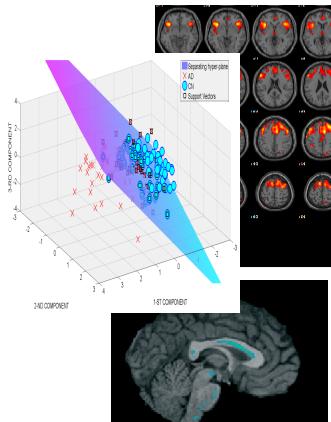


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PET/MRI
machine learning, deep learning

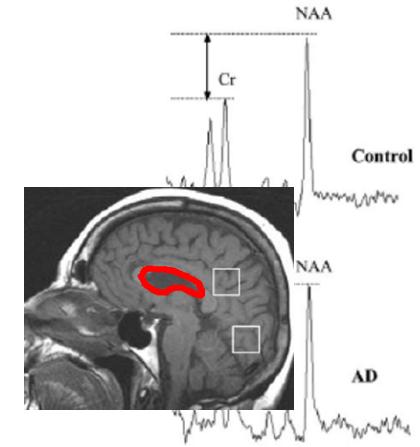


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Annalisa Polidori, PhD

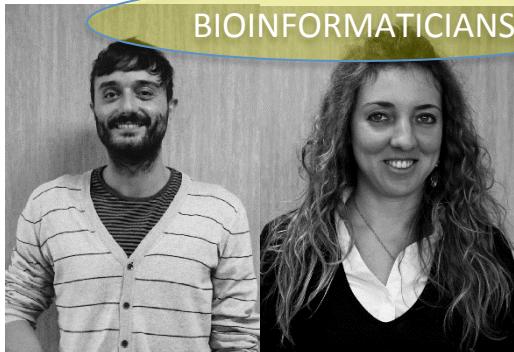
Nuclear Magnetic Resonance
spectroscopy
image segmentation and
deep learning



Competences & Technologies at INLAB[©]

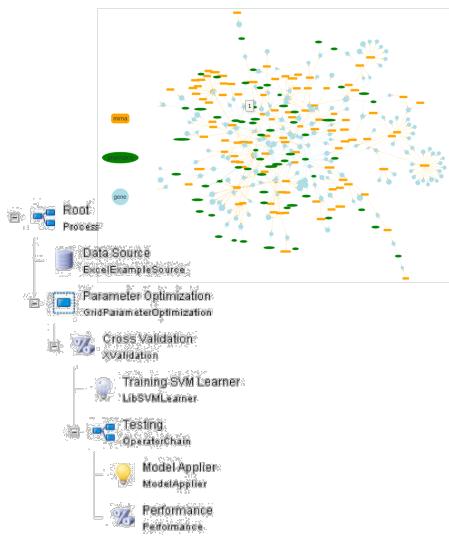


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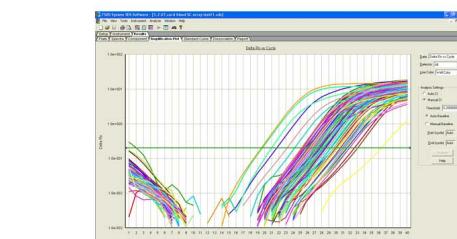
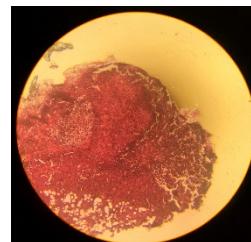


BIOLOGIST



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miRNAs/mRNAs cell studies

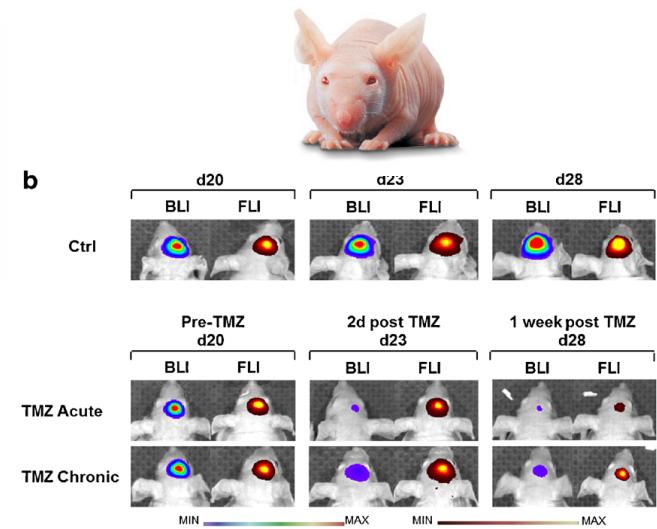


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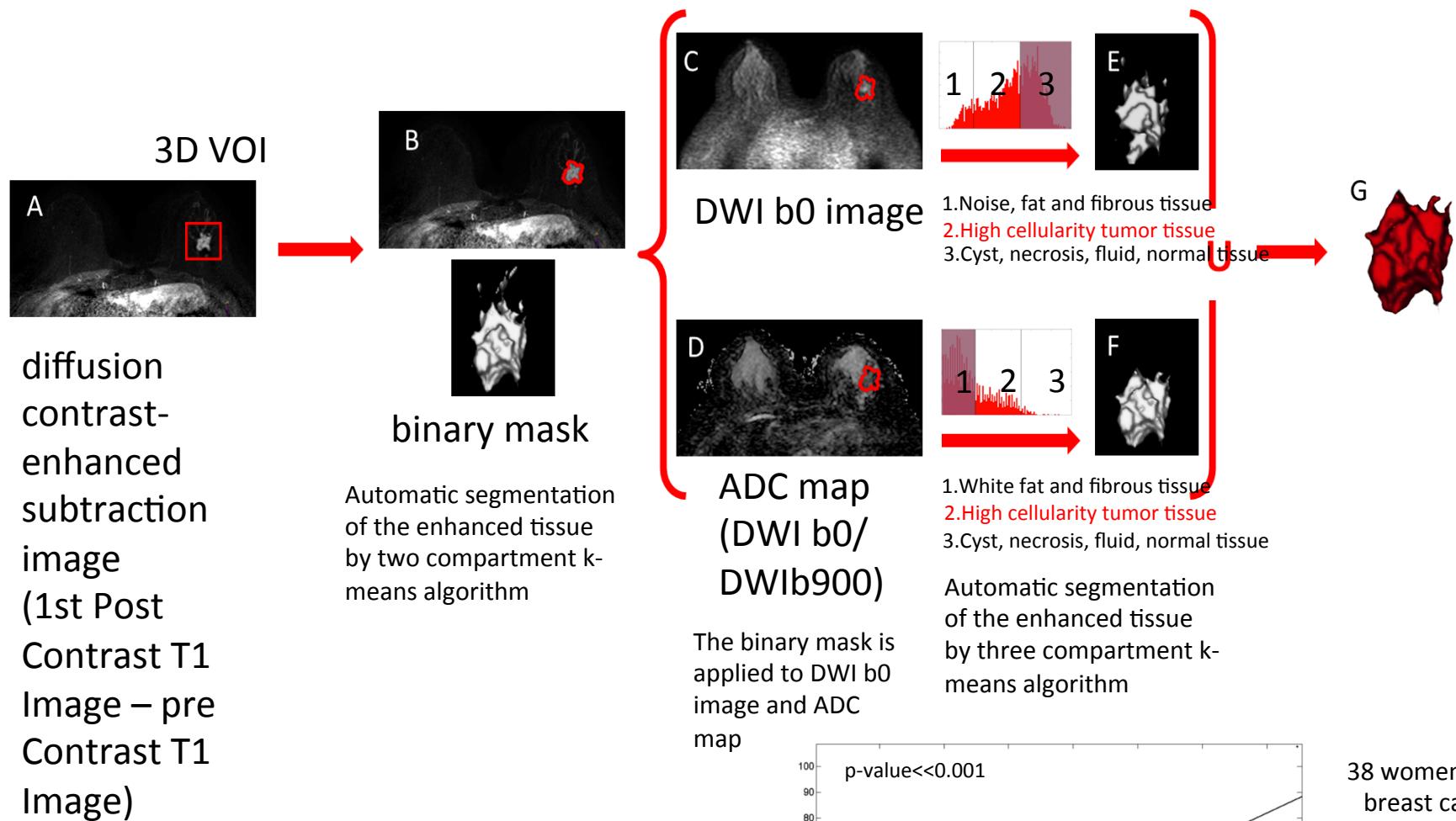
17 projects under formal agreements

The screenshot shows the TCGA homepage. At the top, there's a banner for the "CANCER IMAGING ARCHIVE" showing a surgeon in an operating room. Below the banner is a navigation bar with links: HOME, NEWS, ABOUT US, SUBMIT YOUR DATA, ACCESS THE DATA, RESEARCH ACTIVITIES, and HELP. The main content area features the NIH logo and the text "THE CANCER GENOME ATLAS National Cancer Institute National Human Genome Research Institute". It includes a search bar and links for Home, About Cancer Genomics, Cancers Selected for Study, Research Highlights, Publications, News and Events, and About TCGA. A sidebar on the right contains sections for "Launch Data Portal", "Questions About Cancer" (with links to visit www.cancer.gov, call 1-800-4-CANCER, and use LiveHelp Online Chat), and "Multimedia Library" (with a link to Images).

Thank you for your attention

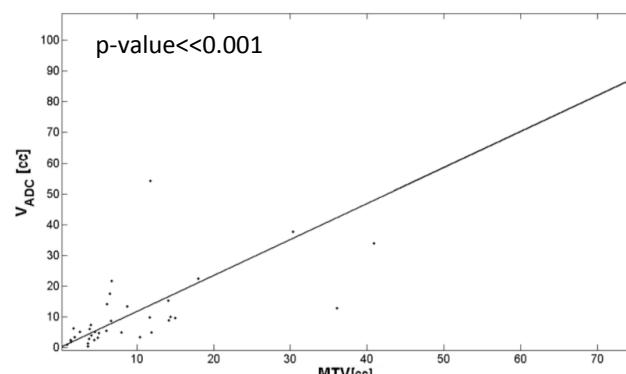
Isabella.castiglioni@ibfm.cnr.it

Accurate estimation of lesion volume: MRI problems



Improvement of the method by

Gong NJ, Wong CS, Chu YC, Guo H, Huang B, Chan Q. Increasing the accuracy of volume and ADC delineation for heterogeneous tumor on diffusion-weighted MRI: correlation with PET/CT. Int J Radiat Oncol Biol Phys, 2013



38 women with breast cancer performing both a 18F-FDG PET/CT and MRI (T1 and DWI) for staging