Artificial intelligence in medicine from genomic to personalize medicine

Maurizio Polano
IRCCS CRO AVIANO
Experimental and Clinical Pharmacology Division

- Develop precision medicine approach based on genomic and molecular profile of the tumour.
- Develop clinical trials (phase 1-phase 2)
- Develop nano drugs and therapies using CART cells.
- Develop computational approach on big data for personalised medicine
Inferno - Canto ventesimo

Da Wikipedia, l’enciclopedia libera

Il canto ventesimo dell’Inferno di Dante Alighieri si svolge nella quarta bolgia dell’ottavo cerchio, ove sono puniti gli indovini e i maghi; siamo all’alba del 9 aprile 1300 (Sabato Santo), o secondo altri commentatori del 26 marzo 1300.

Dante, dopo una descrizione generale, indica tra i peccatori, attraverso le parole di Virligio, cinque indovini antichi (quattro dei quali mitologici) e tre moderni. Durante la presentazione dell’indovina Manto c’è una lunga digressione sulle origini di Mantova.
Personalized medicine vs Precision Medicine

• Personalised medicine is an emerging practice of medicine that uses an individual’s genetic profile to guide decision made in regard to the prevention, diagnosis and treatment of disease.

• Precision medicine are term more appropriate for the description of the approach the focus is on identifying which approaches will be effective for which patients based on genetic, environmental, and lifestyle factors.

• Pharmacogenomics is the study of how genes affect a person’s response to particular drugs.
DATA
Make knowledge from comics
- Health records
- Pathology Images
- Drugs
- Genomic Data

KNOWLEDGE
Predict clinical phenotype

ACTION
Select optimal therapy
Therapeutic Window and Therapeutic Index

- Peak of effect
- Side-effect
- Adverse response
- Therapeutic window
- Desired response
- Sub-therapeutic

Plasma concentrations vs Time
GLIOBLASTOMA

Glioblastoma (GBM) is a devastating disease for both patients and caregivers.

It is the most aggressive primary brain tumour – a tumour that originates in the brain – and despite available therapies, prognosis is extremely poor.

The majority of patients do not survive for more than two years following diagnosis, and the median survival is generally less than a year.¹

The average 5-year survival rate is less than 3%
Standard treatment based on surgery, radiotherapy with concomitant temozolomide followed by 6 or more cycles of adjuvant temozolomide: medial overall survival (OS) is 14.6 months, progression free survival (PFS) 6.9 months (Stupp et al 2005)
GLIOBLASTOMA

Udine Hospital Neurosurgery
Radiogenomics is a relatively recently coined term to denote the relationship between the imaging features of a particular disease and various genetic or molecular features. The former is referred to as an imaging phenotype, whereas the later as genomic phenotype.

Radiogenomics, therefore, provides a tool for clinicians to correlate imaging traits to molecular markers of diseases processes (such as cancer) in an effort to guide tailored therapy.
Machine learning and glioma imaging biomarkers

Table 1
Recent studies applying machine learning to the development of neuro-oncology prognostic biomarkers.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Prediction</th>
<th>Dataset</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cha et al., 2014</td>
<td>Early progression</td>
<td>3 CBV &amp; ADC</td>
<td>Retrospective</td>
<td>Multivariate logistic regression, longitudinal subtraction of ADC &amp; CBV histograms</td>
</tr>
<tr>
<td>Park et al., 2015</td>
<td>Early progression</td>
<td>162 (training = 108 &amp; testing = 54) DWI, ECI, DCE</td>
<td>Retrospective</td>
<td>Sensitivity: 86%</td>
</tr>
<tr>
<td>Kim et al., 2015</td>
<td>Early progression</td>
<td>28 (training = 21 &amp; testing = 7) MRI</td>
<td>Retrospective</td>
<td>Sensitivity: 78%</td>
</tr>
<tr>
<td>Yun et al., 2016</td>
<td>Early progression</td>
<td>33 DCE</td>
<td>Retrospective</td>
<td>Sensitivity: 92%</td>
</tr>
<tr>
<td>Arzii et al., 2016</td>
<td>Pseudoprogression</td>
<td>20 longitudinal patients DCE &amp; MRS (training = 29-44 DCE &amp; MRS studies; testing = 19-44 studies)</td>
<td>Retrospective</td>
<td>Sensitivity: 42%</td>
</tr>
<tr>
<td>Tsiarlis et al., 2016</td>
<td>Radiation necrosis</td>
<td>58 (training = 43 &amp; testing = 15) MRI</td>
<td>Retrospective</td>
<td>Sensitivity: 79%</td>
</tr>
<tr>
<td>Qian et al., 2016</td>
<td>Early progression</td>
<td>35 longitudinal DTT</td>
<td>Retrospective</td>
<td>Sensitivity: 91%</td>
</tr>
<tr>
<td>Van-Mergaere et al., 2016</td>
<td>Early progression</td>
<td>29 T1, T1 C, DWI, DSC</td>
<td>Retrospective</td>
<td>Sensitivity: 97%</td>
</tr>
<tr>
<td>Yoo et al., 2016</td>
<td>Early progression</td>
<td>75 MRI, DWS, DSC, DCE</td>
<td>Retrospective</td>
<td>Sensitivity: 85%</td>
</tr>
<tr>
<td>Booth et al., 2016</td>
<td>Early progression</td>
<td>50 feature extraction, 24 (training = 17 &amp; testing = 7)</td>
<td>Retrospective</td>
<td>Sensitivity: 85%</td>
</tr>
<tr>
<td>Kehm et al., 2016</td>
<td>Early progression</td>
<td>14 18F-FET-PET</td>
<td>Retrospective</td>
<td>Sensitivity: 82%</td>
</tr>
<tr>
<td>Nam et al., 2016</td>
<td>Early progression</td>
<td>37 DCE</td>
<td>Retrospective</td>
<td>Sensitivity: 85%</td>
</tr>
<tr>
<td>Jang et al., 2016</td>
<td>Pseudoprogression</td>
<td>78 (training = 59 &amp; testing = 19) T1 C MRI, Age, Gender, MGMT status, DIH mutation, radiotherapy dose &amp; fraction, follow up interval</td>
<td>Retrospective</td>
<td>Sensitivity: 85%</td>
</tr>
<tr>
<td></td>
<td>Pseudoprogression</td>
<td>105 (training = 59 &amp; testing = 46) MRI</td>
<td>Retrospective</td>
<td>Sensitivity: 85%</td>
</tr>
<tr>
<td></td>
<td>Pseudoprogression</td>
<td>95 (training = 65 &amp; testing = 34) T1 C, FLAIR, DWS, DCE</td>
<td>Retrospective</td>
<td>Sensitivity: 96%</td>
</tr>
</tbody>
</table>

Table 2
Future studies applying machine learning to the development of neuro-oncology prognostic biomarkers.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Dataset</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chi et al., 2017</td>
<td>65 prospective DCE</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
</tr>
<tr>
<td>Kehriginger et al., 2018</td>
<td>196 (training = 79 &amp; testing = 117)</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
</tr>
<tr>
<td>Chang et al., 2015</td>
<td>136 (training = 68 &amp; testing = 68)</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.58</td>
</tr>
<tr>
<td>Liu et al., 2019</td>
<td>147 in OMM &amp; DTT</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
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<tr>
<td>Ninomiya et al., 2016</td>
<td>68 T1 C, in OMM, DTT</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
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<tr>
<td>Masuyama et al., 2018</td>
<td>16 (training = 8 &amp; testing = 8)</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
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<tr>
<td>Zou et al., 2017</td>
<td>52 T1 C, FLAIR, T1 FLAIR</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
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<tr>
<td>Debatin et al., 2017</td>
<td>53 per-lesion DCE</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
</tr>
<tr>
<td>Liu et al., 2017</td>
<td>113 (training = 62 &amp; testing = 51)</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
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<tr>
<td>Zou et al., 2017</td>
<td>133 T1 C</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
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<tr>
<td>Li et al., 2017</td>
<td>90 (training = 48 &amp; testing = 42) T1 T1 FLAIR</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
</tr>
<tr>
<td>Chen &amp; Laff, 2017</td>
<td>138 T1 C, T1 FLAIR</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
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<tr>
<td>Inoguchi et al., 2017</td>
<td>67 T1 C</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
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<tr>
<td>Li et al., 2017</td>
<td>50 (training = 28 &amp; testing = 22) T1 T1 FLAIR</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
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<tr>
<td>Kajimoto et al., 2017</td>
<td>60 (training = 30 &amp; testing = 30)</td>
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<tr>
<td>Suh et al., 2017</td>
<td>107 T1 C, T1 FLAIR</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
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<td>Petrides et al., 2018</td>
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<td>Kehriginger et al., 2018</td>
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<td>Chudak et al., 2016</td>
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<tr>
<td>Bar et al., 2018</td>
<td>49 (training = 24 &amp; testing = 24)</td>
<td>Multivariate Cox regression using MRI, pharmacokinetics, &amp; clinical parameters</td>
<td>C-index: 0.62</td>
</tr>
</tbody>
</table>

11F-FET-PET; 18F-fluorodeoxyglucose positron emission tomography; NPS: negative predictive value; T1 C: post contrast T1-weighted; MGMT, 0'-methylguanine-DNA methyltransferase; DIH, doxorubicin dehydrogenase; CNN: convolutional neural network; APA, area under the precision-recall curve; DCE, dynamic contrast-enhanced imaging; MRS, 1H- and 31P-magnetic resonance spectroscopy; SVM, support vector machine; AUC, area under the receiver operating characteristic curve; cCBV, cerebral blood volume; cADC, cerebral diffusivity coefficient; IACU, initial area under the curve; MP, multiparametric; DWI, diffusion-weighted imaging; DSC, dynamic susceptibility contrast weighted; DTT, diffusion tensor imaging; DCE, diffusion contrast imaging.
GlioAI: Automatic Brain Tumor Detection System

Welcome to GlioAI

Choose file, no file chosen

Upload

Diagram showing the process of detecting brain tumors using GlioAI with layers such as Input Image, Feature Maps, Pooling, Convolutions, and Activation.
GLIOBLASTOMA
Machine learning on glioblastoma

S.O.C. GESTIONE DELLE TECNOLOGIE CLINICHE
Head: Ricci Roberto

Nvidia Tesla V100 GPUs.
Machine learning on glioblastoma

Pre-Operative MRI for Neuronavigation

Deep learning is a subset of machine learning consisting of computational units of multiple layers resembling the multilayered human cognition system.

Several studies using deep learning to predict glioma grading, glioma genetic mutation or survival.

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Several studies using deep learning to predict glioma grading, glioma genetic mutation or survival.

Welcome to pyradiomics documentation!

This is an open-source python package for the extraction of Radiomics features from medical imaging. With this package we aim to establish a reference standard for Radiomic Analysis, and provide a tested and maintained open-source platform for easy and reproducible Radiomic Feature extraction. By doing so, we hope to increase awareness of radiomic capabilities and expand the community. The platform supports both the feature extraction in 2D and 3D and can be used to calculate single values per feature for a region of interest (“segment-based”) or to generate feature maps (“voxel-based”).

Deep learning is a subset of machine learning consisting of computational units of multiple layers resembling the multilayered human cognition system.

Several studies using deep learning to predict glioma grading, glioma genetic mutation or survival.

Emanuele Fabbiani
Università di Pavia

RADIOMICS

DEEP LEARNING
Machine learning on glioblastoma

Typical Workflow of Radiogenomic Studies

- **Image Acquisition**
  - MRI scan of brain

- **Image Processing**
  - T1, T1CE, T2, T2-FLAIR images
  - Preprocessing steps: De-noising, Bias Correction, Registration, Skull-Stripping

- **Region of Interest Definition**
  - T1, T1CE, T2, T2-FLAIR images
  - Identification of brain and tumor regions

- **Feature Extraction**
  - Spatial Distribution Atlases
  - Texture Descriptors
  - Co-Occurrence Matrix
  - Grey-Level Image
  - Brain regions: White Matter, Gray Matter, Cerebrospinal Fluid, Enhancing, Non-enhancing, Edema/Invasion
  - Tumor regions: Enhancing, Non-enhancing, Edema/Invasion

- **Data Analysis**
  - Image and feature data analysis

Maurizio Polano - CRO-AVIANO
Machine learning on glioblastoma

<table>
<thead>
<tr>
<th>type</th>
<th>Count</th>
<th>Philips</th>
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<td></td>
<td>Total</td>
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<td>84.0</td>
<td>158.0</td>
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<table>
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<th>Total</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>89.559</td>
<td>89.059</td>
<td>89.392</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>92.5</td>
<td>95.0</td>
<td>95.0</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>96.958</td>
<td>97.222</td>
<td>97.047</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Total Mean</td>
<td>94.562</td>
<td>94.604</td>
<td>94.576</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>98.0</td>
<td>98.0</td>
<td>98.0</td>
</tr>
</tbody>
</table>
Machine learning on glioblastoma

Volume T2 pre

IDH mutation and survival
Machine learning on glioblastoma
Machine learning on glioblastoma

Preprocessing

185 patients anonymous

Ktulu-pod

Kubernels

PyTorch

PyTorch is an open-source machine learning library based on the Torch library, used for applications such as computer vision and natural language processing, primarily developed by Facebook's AI Research lab. It is free and open-source software released under the Modified BSD license. Wikipedia

License: BSD
Developer(s): Facebook's AI Research lab (FAIR)
Original author(s): Adam Paszke, Sam Gross, Soumith Chintal, Gregory Chanan
Stable release: 1.6.0 (28 July 2020); 2 months ago
Initial release: September 2016; 4 years ago
Written in: Python, C++, CUDA
Machine learning on glioblastoma

Hyperparameter tuning vs. model training

Parameters: 17861314
Total Parameters : 5102134
Resnet 18: Transfer learning using Medical Net 50 epoch
OTHER EXPERIENCE: COLON CANCER

A radiomics-based formula for the preoperative prediction of postoperative pancreatic fistula in patients with pancreaticoduodenectomy

Wenwu Zhang 2
Wei Cai 3

Objective: The objective of the study was to develop and validate a radiomics-based formula for the preoperative prediction of postoperative pancreatic fistula (POPF) in patients undergoing pancreaticoduodenectomy.

Table 1: Radiomics calculation formula

<table>
<thead>
<tr>
<th>Term</th>
<th>Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>0.5</td>
</tr>
<tr>
<td>Age</td>
<td>0.7</td>
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<tr>
<td>Body Mass</td>
<td>-0.3</td>
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<tr>
<td>Tumor Size</td>
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</tr>
</tbody>
</table>

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Cancer Management and Research
Dovepress
Open access to medical and surgical research

ORIGINAL RESEARCH

Maurizio Polano - CRO-AVIANO
FUTURE

Next Steps

IDEAS
Progress
Discuss
MEETING
Business
Future
Innovation
Dialog
Forum
Communication

QUESTIONs
Exploration
Connection
Session
INPUT
TALK
Creativity
BUSINESS
FUTURE
PROPOSAL
Strategy

FORWARD
SOLUTIONS
STRATEGY
Thanks all for the Attention