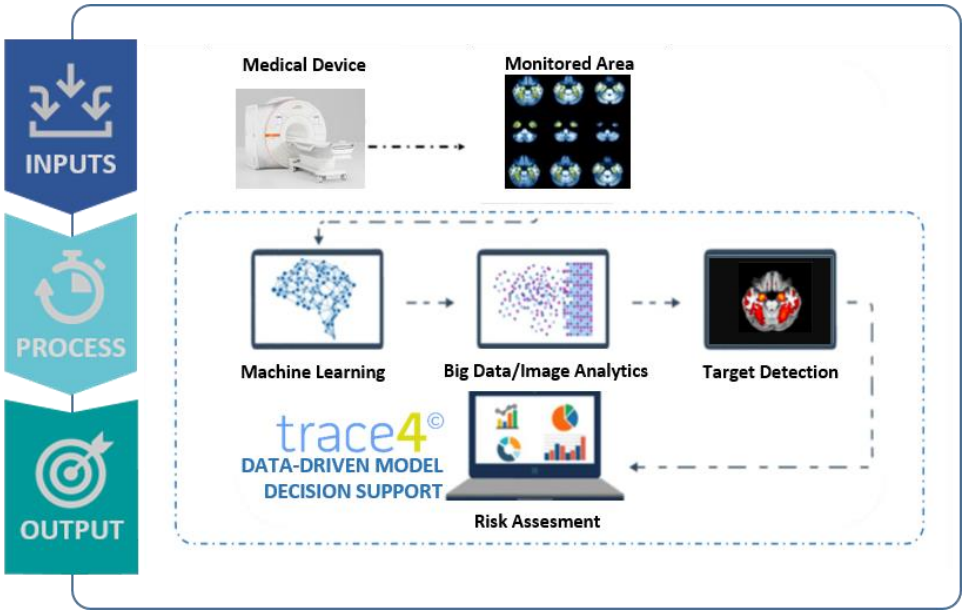
# trace4

Trace4© is a DeepTrace-Technologies proprietary Software-Platform of Radiomics and Artificial Intelligence (AI) for statistical analysis and AI-modeling of medical images. Trace4© is based on open-access and proprietary software to allow

1- Big Data/Image Analytics and storage
2- Development of Radiomics and AI customizable-models and prototypes
3- Data Visualization of clinical outcomes.

The treatment of medical data and images can support the decision and knowledge-management processes in the medical field. Highly specialized algorithms based on Machine Learning, Deep Learning, Transfer Learning, Big Data Analytics and Mining, Image Processing, Image Analytics and Mining, and Texture analysis are offered to clinicians in a user-friendly and robust modality, following a simple workflow.

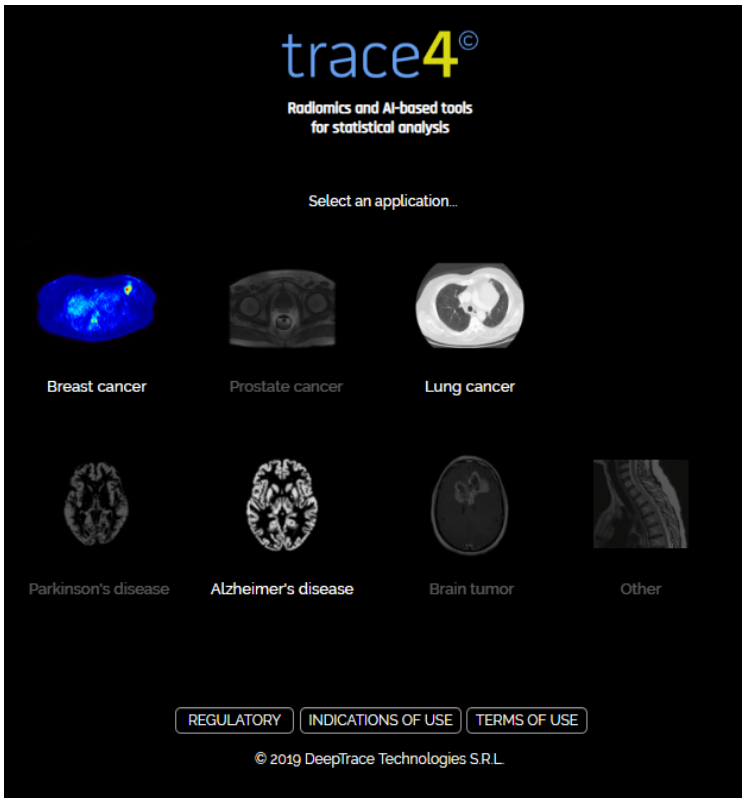



Trace4© Platform offers an integrated data-driven and domain-specific decision-support tool almost in real time. Also, thanks to the "*privacy-by-default*" Security&Privacy settings, the Client/User data are constantly protected during the development and implementation of the Platform services.

# INDICATION OF USE

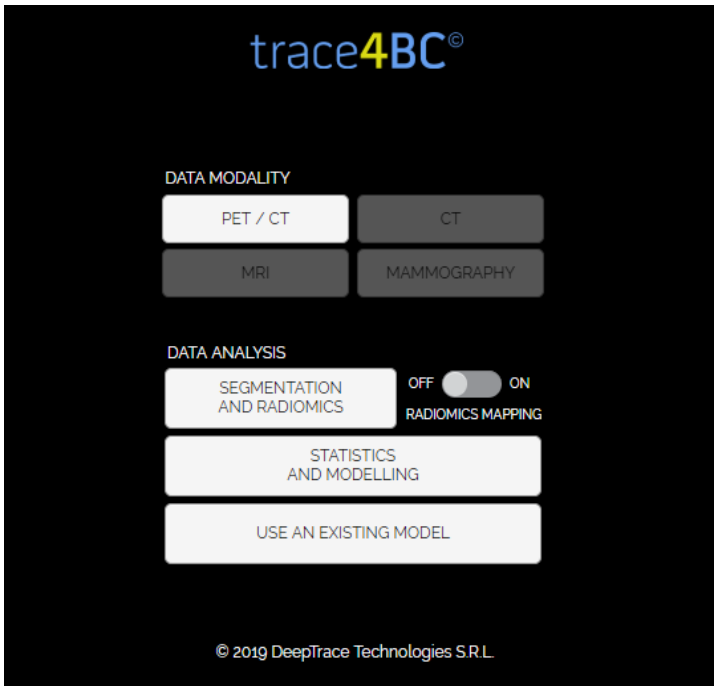
The Trace4© Platform is intended for being used by Radiology or Nuclear-Medicine practitioners, as well as referring physicians. They can use Trace4© for displaying, processing, classifying, archiving, printing, reporting radiology and nuclear-medicine images, image features, including planar and tomographic scans acquired by ultra-sonographers, X-ray, gamma cameras, PET, CT and MRI scanners.

The Trace4© Platform can be deployed on dedicated workstations or in a server-client configuration as stand-alone application (on Microsoft Windows operating systems).



# TECHNICAL DESCRIPTION

Images from ultra-sonographers, X-ray, gamma cameras, PET, CT and MR scanners can be coupled with feature extraction methods, eventually using Volume-of-interest (VOIs), in order to depict, localize, and/or quantify the heterogeneity and morphology in anatomical/functional structures or in the distribution of radionuclide tracers in scanned body tissue for research and statistics purposes.



# SEGMENTATION AND RADIOMICS

The “Segmentation and Radiomics” application-option enables quantification, archiving and displaying of radiomic features from VOI-based segmented portion of a planar or tomographic scan.

Radiomic features are quantitative measures of body-tissue heterogeneity and morphology of the VOIs-based segmented portion of images, expressed in terms of Morphology, Intensity-based Statistics, Intensity Histogram, Gray-Level Co-occurrence Matrix (GLCM), Gray-Level Run Length Matrix (GLRLM), Gray-Level Size Zone Matrix (GLSZM), Neighborhood Gray Tone Difference Matrix (NGTDM), Gray-Level Distance Zone Matrix (GLDZM), Neighboring Gray Level Dependence Matrix (NGLDM). Their definition, computation and nomenclature are compliant with the International Biomarker Standardization Initiative (IBSI) guidelines [https://arxiv.org/abs/1612.07003]. In the case of 2D images, the features of the family Morphology, originally designed by IBSI for 3D tomographic images, are replaced with 2D equivalent features (e.g. 3D features volume and surface are replaced with 2D features area and perimeter, respectively). Resampling to isotropic voxel spacing, and intensity discretization are performed prior radiomic features measurement.

# RADIOMIC STATISTICAL ANALYSIS AND MODELING

Radiomic statistical analysis and modeling application-option enables statistical multivariate analysis on radiomic features from image VOIs at level of groups of images or single-image.

The selection of radiomic features, stable across groups of images with respect to different segmentations and repeatable in test-retest study, are performed by statistically comparing features obtained by data augmentation strategies and selecting those with Intra-Class Correlation Coefficient (ICC) >0.80: a) randomly manipulating the segmentation of the image VOIs, and b) rotating the original images and segmentations. The selected radiomic features (stable and repeatable across groups of images) can be used for statistical multivariate analysis at the level of single-image.

Different systems of machine-learning classifiers can be trained, validated, and tested as multivariate model for a binary-classification task (images from group 1 vs images from group 2, based on the supervised training by the user), reducing the more stable and reproducible features to not-redundant features, in a number of degrees of freedom appropriate with respect to the number of collected images (approximately 1 feature every 10 images). One of the machine-learning system is an ensemble of 200 Decision Trees combined with Gini index with majority vote rule; another machine-learning system is an ensemble of 100 Support Vector Machines combined with Principal Components Analysis and Fisher Discriminant Ratio with majority vote rule. For each system, nested K-fold cross validation method is used (default value k=10). Oversampling technique for the minority class is applied by adaptive synthetic sampling method. The performances of the different classification systems are measured across the different folds (k=10) in terms of max and mean Accuracy, Sensitivity, Specificity, AUC and standard deviation. The classification system with the best performances is selected as the best classification system for the binary task of interest at the level of single-image (image from class1 vs images from class2, based on the supervised training by the user). The best radiomic features (more stable, reproducible, not redundant and accurate in the classification task) are obtained.

# RADIOMIC MULTIVARIATE MODELING

The use of Radiomic Multivariate model application-option enables statistical multivariate analysis on radiomic features from image VOI at level of single-image using the best classification system for the binary classification task (image from group 1 vs image from group 2). The use of multivariate model option may support in detection and quantification of tissue heterogeneity and morphology of image VOI which can be associated with diagnosis, prognosis and response to treatment of the scanned body tissue.

# DEEP LEARNING MODELING

Deep-Learning Modeling application-option enables 1) training deep-learning classifiers based on features learnt from images belonging to different classes of interest, 2) classifying new images based on deep-learning models previously trained on the Platform.

Deep-learning models can be trained, validated, and tested for both binary and multiple-classification tasks, based on the supervised training adopted by the user.

Deep-learning architectures adopted for image analysis are based on convolutional neural-networks (CNNs) composed of many layers whose aim is to learn a rich feature-representation of the input classes, and to use this representation to classify new images as belonging to one of the input classes.

Deep-learning architectures can also be obtained by pre-trained open-access CNNs and fine-tuned (Transfer Learning) in their last layers for the task of interest.

In order to increase medical image-diversity among different training phases (epochs), automatic data-augmentation techniques (including image rotation, shear and reflection) can be applied to the images during the training of the classifier.

Performances of the deep-learning classifiers can be measured, also across different folds when a cross-validation approach is adopted, in terms of max and mean Accuracy, Sensitivity, Specificity, AUC and standard deviation.

## REGULATION

Trace4© has been developed in accordance with the GDPR (General Data Protection Regulation 2016/679) considering privacy by default in the design.

Trace4© is not a medical device. It is not CE marked nor FDA cleared as medical device. Any use of this software and the associated information is for research and statistical-analysis purposes only.

## TERMS OF USE AGREEMENT

Acceptance of Agreement. The user agrees to the terms and conditions outlined in this Terms of Use Agreement ("Agreement") with respect to the software suite “Trace4©" created by DeepTrace Technologies S.R.L. (the "software”).
Intellectual Property. Limited License to Users. Any unauthorized use of the Materials, Content or Tools within this Software may violate laws and the Terms of Use. The user agrees not to copy, republish, frame, download, transmit, modify, rent, lease, loan, sell, assign, distribute, license, sublicense, reverse engineer, or create derivative works and tools based on this Software, its Materials, Content or Tools or their selection and arrangement, except as expressly authorized herein by DeepTrace Technologies S.R.L. The user agrees that will not decompile, reverse engineer, or otherwise attempt to discover the source code of this software.
Limited Right to Use. The viewing, using, printing or downloading of any Material, Content, Graphic, Form or Document from this software grants the user only a limited, nonexclusive license for use solely by the purpose defined under the Contract with DeepTrace Technologies S.R.L, and not for republication, distribution, assignment, sublicense, sale, preparation of derivative works or other uses unauthorized by DeepTrace Technologies S.R.L. No part of any content, form or document may be reproduced in any form or incorporated into any information retrieval system, electronic or mechanical, other than for the use defined under the Contract (but not for resale or redistribution). The rights granted to the user constitute a license and not a transfer of title.