PRIMAGE

Medical imaging
Artificial intelligence
Childhood cancer research

D4.1 – Generation of radiomic data from retrospective sets

Project Full Title: *PRedictive In-silico Multiscale Analytics to support cancer personalized diaGnosis and prognosis, Empowered by imaging biomarkers.*
Project acronym: *PRIMAGE*
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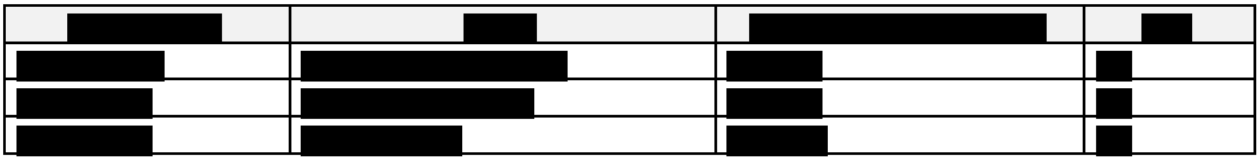

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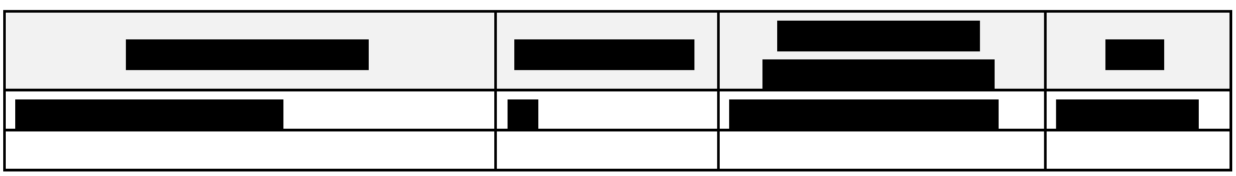

1. INTRODUCTION

The goal of this deliverable is to report about the extraction of radiomic data from a retrospective set of medical images. The areas of application have focused on two paediatric cancers: neuroblastoma (NB) [1] and diffuse intrinsic pontine glioma (DIPG) [2].

1.1 Key points

Radiomics [3] is an emerging translational field of research aiming to extract mineable high-dimensional data from clinical images. The radiomic process can be divided into distinct steps with definable inputs and outputs, such as image acquisition and reconstruction, image pre-processing (denoising, registration, segmentation…), features extraction and quantification, analysis, and model building. Each step needs careful evaluation for the construction of robust and reliable models to be transferred into clinical practice for the purposes of guiding clinicians in the diagnosis, prognosis, non-invasive disease tracking, and evaluation of disease response to treatment.

This deliverable summarises the major issues regarding this multi-step process, focussing in particular on challenges in the extraction of radiomic features from data sets obtained from magnetic resonance (MR) imaging and computed tomography (CT).

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5. CONCLUSION

The image processing pipeline developed within the PRIMAGE project was optimized to address different problems such as image motion, noise and intensity inhomogeneity, some of them being particularly challenging in paediatric cancer imaging. This pipeline is expected to evolve over time to incorporate future improvements and extensions in order to better address the challenges of large-scale multimodal image processing and analysis (e.g. harmonisation of images among different machines and data collection techniques), including the use of deep learning techniques and the incorporation of image metadata.

A pipeline for the intra-patient registration of multi-modal imaging data (T2-weighted, DWI-MRI, DCE-MRI, CT, PET/CT) was developed to transfer the images to the same coordinate space before subsequent analysis. The registered images were controlled for their accuracy, both in a qualitative and in a quantitative way. For the cases where the registration was not accurate, the registration was repeated by adding a mask of the tumour areas and / or adjacent organs in order to help the registration procedure. Nonetheless, the registration of multi-modal imaging data is a particularly challenging task due to motion artefact, low image quality and variability in acquisition. For this reason, further improvements on the already acquired results as well as other approaches (i.e. diffeomorphic registration) and the options for manual registration (ITK-SNAP 3.8.0, Osirix) when automatic registration is not accurate will be further investigated.

Manual segmentations of the neuroblastoma and DIPG tumours were produced for the current dataset by two experienced radiologists using the T2-weighted and T1-weighted images, respectively. Moreover, the set-up and first trials to use the manual segmentations to train a deep convolutional neural network (UNET combined with deep supervision) to be used to automatically segment the neuroblastic and DIPG tumours in unseen images was performed. Currently, different state-of-the-art open-source network solutions are being explored and compared in terms of their achieved accuracy. The first results were obtained, but the currently limited size of our dataset along with the inherent challenges of segmenting both neuroblastoma and DIPG (missing borders, variability in shape and location) limits the performance

of the existent algorithms. Therefore, the development of novel approaches is necessary and will be explored.

Radiomic and deep features were extracted from T1/T2-weighted, DWI and DCE MR images, as well as from CT and MIBG data sets. We are currently experiencing a paradigm shift to a symbiosis of computer science and radiology using artificial intelligence integrated with machine and deep learning with radiomics to better define tissue characteristics. Our next goal in the project is to use integrated deep learning and radiomics with radiological parameters to produce a personalized diagnosis for a patient, with the objective of minimizing our current biases and limitations. The dataset size, which at the moment represents a large uncertainty source, will be massively increased in the upcoming months.

Most MR derived dynamic metrics, like the monoexponential ADC calculation and the semi-quantitative DCE MR parameters, are performed voxel-by-voxel and then the metric is averaged. This approach gives a mean tumour value but has several limitations, mainly related to the low signal-to-noise ratio of the pixels, the signal uncertainty within voxels due to partial volume effects, the heterogeneity of tumours and the use of average values as representatives. The use of larger multivoxel regions to provide with this metric allows better signal to noise and signal fitting for the defined region, but uncertainty is now cantered of this region definition. We proposed a two steps approach to deal with these limitations. First, voxel uncertainty is considered and voxels with high uncertainty values excluded, being more homogeneous and representative habitats selected. Then, these regions behave like a ROI were signal is averaged and then fitted to have a robust estimate of the selected parameter, the ADC and the initial AUC after 60 seconds, in our case.

The proposed innovative and novel *Fit-Cluster-Fit* methodology has been observed to successfully differentiate benign and malignant neuroblastic tumours in terms of the ADC (p-value = 0.00166). This work lays the foundation for future advances in reproducible imaging biomarkers [21] for paediatric solid tumour cancers and can be extended to any tumour dynamic signal evaluation.