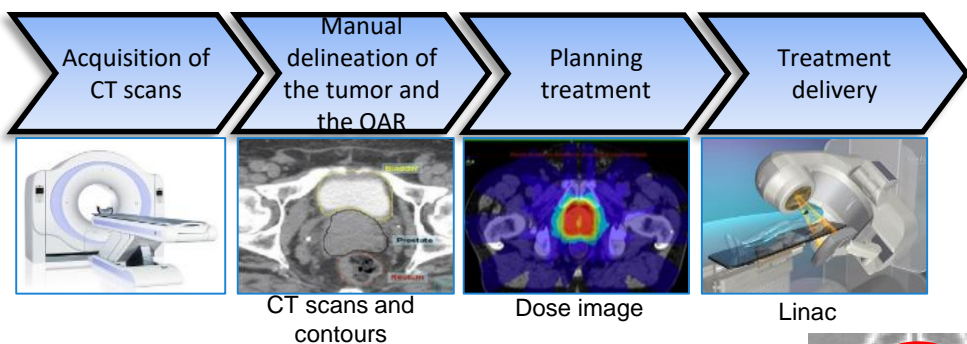


Scientific context

Cancer leading cause of death worldwide (10 million deaths in 2020), radiotherapy is one of the cancer treatment.

Workflow of external radiotherapy (RT):



- CT-Scan: reference imaging for dose planning in radiotherapy (RT)
 - poor contrast in soft tissues and ionizing imaging
 - imprecise delineation of the tumor and the organs at risk (OARs)
 - limiting the quality of the daily patient treatment positioning
- MRI: better soft tissue contrast compared to CT
 - but MRI do not provide electronic density information necessary for dose calculation
- State of art MR-to-CT synthesis: deep learning methods (DLM) [Boulanger21]

Limitation of DLM-based MR-to-CT synthesis:

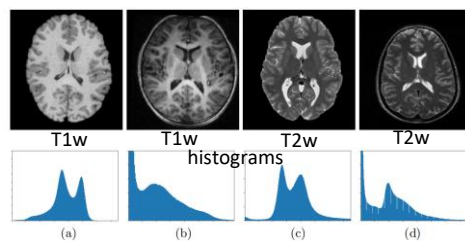
- variety of image acquisition systems (manufacturers, calibration, acquisition parameters, magnetic field, etc.)
 - training data specific to CT/MRI device [Boulanger21]

Goals :

- Generation of synthetic CT (sCT) from MRI, based on DLM
- Development of a generic approach taking into account the variety of image acquisition systems
- Combine several 3D MR sequences (T1, T2, resolution, LavaFLEX, etc.)
- Develop supervised and unsupervised learning

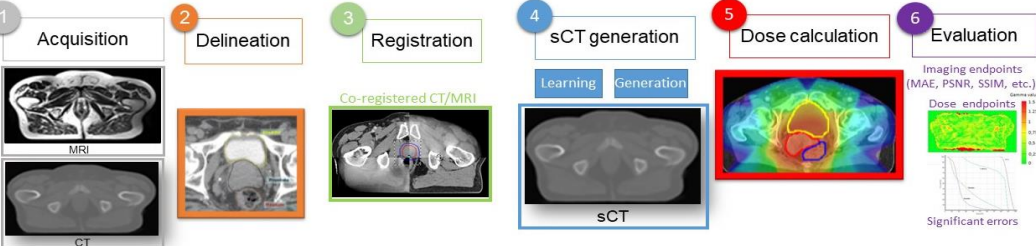
Data :

- Prostate and brain cancer: 3D CT, 3D MRI (T2, LavaFLEX) from Centre Eugène Marquis (CEM), Centre Régional de Lutte Contre le Cancer (CLCC) de Rennes.



Workflow of the study (Work Packages):

Workflow of the study presenting the different steps (WP1 to WP6):



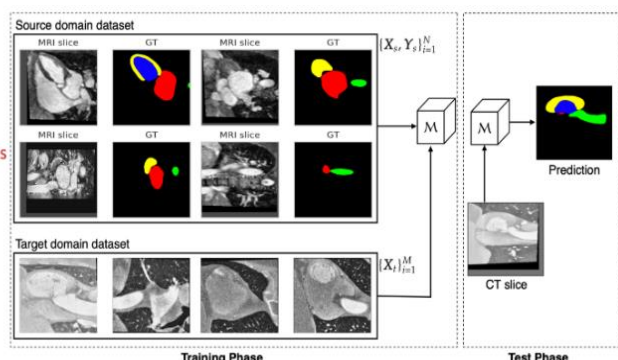
Automatic segmentation and uncertainty WP2

Automatic segmentation (LS2N, Nantes)

- Anatomical regions: **prostate** + OARs (rectum, bladder) and **brain** + OARs (medulla, brainstem, pituitary gland, lens, eyes, retina, chiasm, optic nerve).
- Joint segmentation across different MR sequences (T1 and T2, LavaFLEX): exploit all data available.

Challenges:

- Structures not visible on CT for dose computation: build on unsupervised and weakly supervised domain adaptation [AlChanti21a] to transfer segmentation of soft tissues from MR to CT.
- Associate an uncertainty measurement to the predictions [Jimenez22].



OLVA Optimal Latent Vector Alignment [AlChanti21a] relies on a VAE (Variational Autoencoder) and Optimal Transport to align the latent vector representation of organ shapes from two modalities.

Image registration (MRI/CT and MRI/MRI) WP3

Image registration (LS2N and LTSI):

To match patient anatomy between CT and MRI

Method: a multimodal non-rigid registration approach (MRI/CT) guided by segmentation. Explore hybrid optimization and deep learning based approaches [Fourcade22]

Evaluation of image registration will be based on:

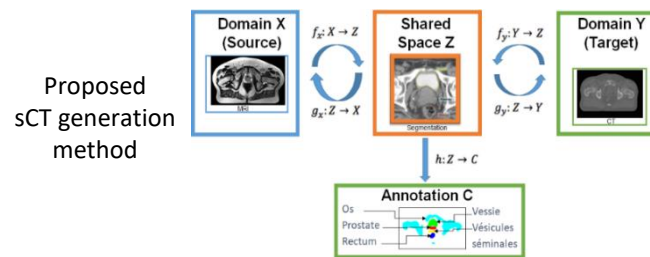
- Iconic measures: Mutual Information (MI), Structural Similarity (SSIM), Modality Independent Neighbourhood Descriptor (MIND)
- Geometric measures based on delineated structures using dice score coefficients (DSCs), Hausdorff distance (HD) and normalized cross-correlation (NCC).

Multicentric MRI-to-CT generation WP4

DL-based sCT generation method (LTSI)

MR-to-CT generation based on DLMs in multi-center context

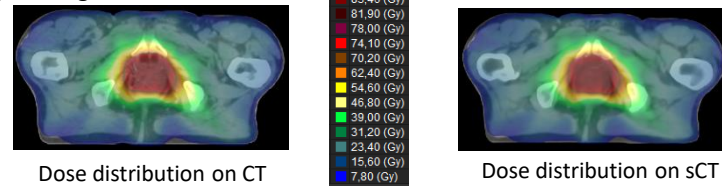
- from several MR images, multiple inputs (named multi-input single-output (MISO)) [Koike20]
- supervised learning with registered paired MR and CT volumes
- unsupervised (unpaired MR and CT) learning methods [Hoffman17, Hiasa18]
- domain adaptation methods [Wilson20, Guan21, Murez18]



Dose calculation WP5

Dose Calculation (LTSI):

- Use of treatment planning system (TPS) Raystation (Raysearch) at Centre Eugène Marquis
- Dose planning on CT and transfer of beam characteristics on sCT



Evaluation WP6

Standardizing the sCT evaluation (LTSI)

- Imaging endpoints based voxel-wise comparison (sCT vs CT): Mean Absolute Deviation (MAE), Mean error (ME), PSNR, Structural Similarity Metric (SSIM), Visual Information Fidelity (VIF),
- Dosimetric endpoints: voxel-to-voxel dose difference (between dose calculated on CT (reference) and on sCT), dose-Volume Histogram (DVH) differences, Gamma-index analyses (comparison of dose distributions)
- Voxel-wise statistical test (Chen permutation test) will be applied on images and on dose distributions [Chourak21].

Expected results and medical potential impact

- Increase the quality of delineation of the target volume and OAR from the MR-image;
- Development of a non-specific center/device, accurate and fast learning of DLM to generate sCT from MRI → accurate dose calculation from MRI (with sCT)
- Avoid the CT acquisition step for patient RT workflow: decrease delineation and registration uncertainties, that could reduce toxicities and increasing local control
- Improve the state of the art in DLMs for sCT generation and joint segmentation-registration;
- Lead to patents and scientific communications/publications.

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