DOCTORAT BIOLOGIE BRETAGNE SANTE LOIRE

Year 2022

THESIS TOPIC

Subject N° (to be completed by the ED):	**FUNDING:** x **Requested** ☐ **Acquired**	**Funding origin:** Funding Ligue contre le Cancer - Région Bretagne
Thesis title: Longitudinal follow-up of liver metastases from colorectal cancer using artificial intelligence		3 keywords: longitudinal follow-up, deep learning, oncology
Unit / team: LaTIM U1011, Inserm | ACTION team - https://latim.univ-brest.fr		
Supervisor's names: - director : Dr Bogdan Badic, MD, PhD - CHRU de Brest, UBO, LaTIM U1101 - co-supervisor : Dr Pierre-Henri Conze, associate Professor - IMT Atlantique, LaTIM U1011		Phone number: +33 6 36 47 01 77 Email: bogdan.badic@chu-brest.fr

Socio-economic and scientific context:

The management of patients with colorectal cancer, the second most common cause of cancer deaths, is a major public health issue. Approximately half of patients with colorectal cancer develop a distant recurrence. The liver, via the development of liver metastases, is the most common site of spread, accounting for 15-25% of patients at diagnosis and a further 18-25% of patients within 5 years. The objective is to find a management adapted to each patient by integrating individual (age, comorbidity, stage...), tumoral (number, size, position...) and collective data. With an estimated 5-year survival rate between 37% and 58%, liver resection consists of the complete removal of lesions, leaving at least 30% of the parenchyma. When surgery is not an option, the treatment regimen consists of palliative oncological treatments. Computed Tomography (CT) image analysis is a crucial step in assessing the response to chemotherapy treatments. Most assessment methods are based on measures related to lesion size. In particular, RECIST criteria are the most commonly used morphological criteria. New radiomic criteria exploiting homogeneity, contours, texture or density information from the main lesion have recently shown an early prognostic contribution for both assessment of treatment response and survival prediction. However, these assessments require accurate delineation of liver metastases. This task is time consuming and subject to high intra- and inter-expert variability. The contribution of medical image analysis in this context represents a key prospect for improving, automating and predicting the therapeutic follow-up.

Working hypothesis and aims:

We hypothesise that the development of deep learning-based tools dedicated to the characterization and the prediction of pathological tissue evolution, in relation to the selected therapy, can greatly guide clinicians in their medical image interpretation tasks. The following questions arise. Can we improve therapeutic follow-up through longitudinal image analysis? Can we accurately predict pathological evolutions using deep learning? Can we find early biomarkers of chemotherapy response and survival? In this context, we aim at developing deep learning methods able to characterise and predict the evolution of pathological structures from follow-up CT scans.

Main milestones of the thesis:

The thesis will be structured in 3 steps: (a) segmentation of liver lesions from CT images, (b) automatic evaluation of the response to chemotherapy and (c) prediction of the pathological evolution using deep learning.

(a) Based on the LaTIM's expertise in abdominal image segmentation, we will first develop a deep learning segmentation model combining convolutional networks and Transformers to achieve automatic, reliable and reproducible delineation of liver and liver metastases visible from baseline and follow-up CT scans.

(b) These delineations will then allow an automated measurement of the metastatic progression over time to be obtained and validated, in order to provide the response to chemotherapy without interaction. This will improve patient management by standardising the RECIST assessment (which often differs between radiologists) and studying other parameters to refine the treatment response evaluation.

(c) We will finally try to extract typical patterns of pathology evolution to optimize the therapeutic follow-up of colorectal cancer patients with hepatic metastases. Beyond the RECIST evaluation, the objective will be to find early markers of response to chemotherapy and progression-free survival. Our contributions will support the development of a patient-specific chemotherapy regimen recommendation system.

More generally, the research lines will aim at providing decision support tools in oncology to guide clinicians in the therapeutic management of colorectal cancer patients with liver metastases. The work will benefit from the availability of databases collected at the Brest University Hospital as well as data obtained through the French Federation of Digestive Oncology (FFCD) and arising from both PRODIGE 9 and PRODIGE 20 clinical trials.

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Scientific and technical skills required by the candidate:

Required skills: 1- solid theoretical and practical knowledge in applied mathematics, (medical) image processing and deep learning, 2- Python programming, 3- rigour and organisational skills, 4- good proficiency in English for reading/writing scientific articles, 5- strong interest in the field of healthcare.

3 publications from the team related to the topic:

Bogdan Badic et al. "Prediction of recurrence after surgery in colorectal cancer patients using radiomics from diagnostic contrast-enhanced computed tomography: a two-center study." European Radiology, pp.405-414, 2022.

Pierre-Henri Conze et al. "Abdominal multi-organ segmentation with cascaded convolutional and adversarial deep networks." Artificial Intelligence in Medicine, 2021.

Bogdan Badic et al. "Radiogenomics-based cancer prognosis in colorectal cancer." Scientific Reports, 2019.

National and international collaborations:

The research axes described above will allow the continuation of the activities in learning-based abdominal image analysis initiated between LaTIM UMR 1101, IMT Atlantique, CHRU Brest and CHU Poitiers. The planned collaboration is characterised by the ambition to propose not only methodological contributions but also to contribute to concrete cases of applications in oncology. Interactions with Sophia Genetics, ICube (Strasbourg) and CREATIS (Lyon) laboratories will increase the visibility of the actions carried out in the framework of the PhD thesis. This project will benefit from the expertise of CHRU Brest (visceral and digestive surgery) and CHU Poitiers (diagnostic, functional and therapeutic imaging centre) with a view to collecting datasets and validating methods from a clinical point of view. The work carried out will also benefit from the collaboration with the Dokuz Eylul University, Izmir, Turkey.