ALMA MATER STUDIORUM · UNIVERSITY OF BOLOGNA

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**Master Degree in Physics**

# Implementation of an automated pipeline for predicting the response to neo-adjuvant chemo-rediotherapy of colorectal cancer

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**Abstract**

Colorectal cancer is a malignant neoplasm of the large intestine resulting from the uncontrolled proliferation of one of the cells making up the colorectal tract.
In Western countries, colorectal cancer is the second largest malignant tumor after that of the breast in women and the third after that of the lung and prostate in men. Risk factors for this kind of cancer include colon polyps, long-standing ulcerative colitis, diabetes II and genetic history (HNPCC or Lynch syndrome). In order to get information about diagnosis, therapy evaluation on colorectal cancer, analysis on radiological images can be performed through the application of dedicated algorithms.
In this scenario, the correct and fast identification of the cancer regions is a fundamental task. Up to now this task is performed using manual or semi-automatic techniques, which are time-consuming and subjected to the operator expertise.
The aim of this project is to provide an automated pipeline to predict the response to neo-adjuvant chemo-radiotherapy of patients affect by colorectal cancer.

*. . . To my family and Nicole*

# Contents

# Introduction

Colorectal cancer is a malignant neoplasm of the large intestine resulting from the uncontrolled proliferation of the cells making up the colorectal tract. Colorectal cancer is the second malignant tumor per number of deaths after the lung cancer and the third for number of new cases after the breast and lung cancer[1].
Among the risk factors for this kind of cancer, non hereditary could range from colon polyps to long-standing ulcerative colitis, from Crohn's disease to old age. Also genetic history (HNPCC or Lynch syndrome) and nutritional factors as diabetes II can increase the probability of develop cancer [2]. Preventive measures for colorectal cancer include physical activity, reducing the consumption of processed meat and alcohol, and avoiding smoking[3].

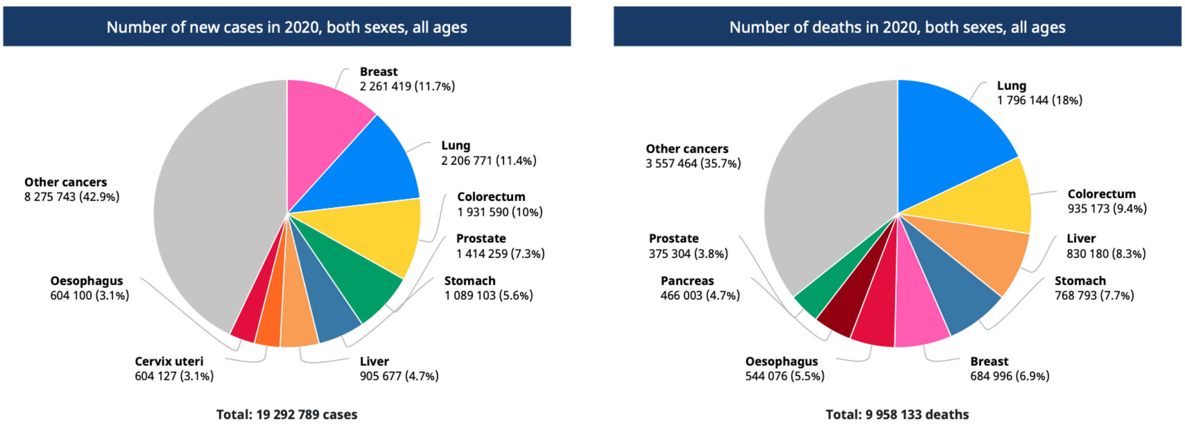


Figure 1: World's cancer cases and deaths. From [1]

Screening and diagnosis methods for colorectal cancer can be based on different techniques. The gold standard in medical routines is colonoscopy which is an invasive technique[4]. Among medical imaging techniques, Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are the most used[2]. In particular Magnetic Resonance

Imaging (MRI) is used for pre-operative predictions and for the evaluation of the neo-adjuvant therapy of patients affected by colorectal cancer [2].

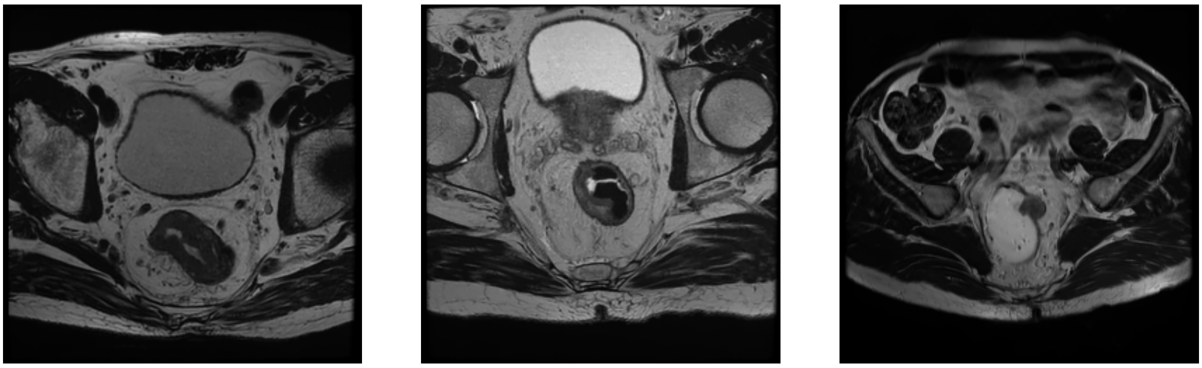

Figure 2: Example of MRI scans of patients affected by colorectal cancer. From Sant'Orsola original Dataset.

In order to get information about diagnosis, therapy evaluation, stage of colorectal cancer, analysis on radiological images can be performed through the application of dedicated algorithms.
In this scenario, the correct and fast identification of the cancer regions is a fundamental task. Up to now, this segmentation task is performed using manual or semi-automatic techniques, which are time-consuming (requiring hours per day) and subjected to the operator expertise since it requires the interaction with trained specialists[2, 4]. Moreover, due to the highly sensitivity to the operator expertise, the obtained results cannot be reproduced[5]. To overcome these issues, an automatic and fast way is required.
The aim of this project is to provide an automated pipeline to predict the response to neo-adjuvant chemo-radiotherapy of patients affect by colorectal cancer. The work is based and tested on MRI scans provided by IRCCS Sant'Orsola-Malpighi Policlinic.
The discussion will start focusing on medical digital images to understand their properties and features. After that, an overview on the main segmentation method for the identification of the cancer regions will be given. Then, the main pipeline characteristics and structure will be described. In particular, how the segmentation was achieved using a Convolutional Neural Network and how extracting and processing medical image features. Finally, the result will be shown and discussed.

Chapter 1

# Medical Digital Images

A medical digital image is the representation of the anatomical (or functional) structure of the patient composed by a finite number of picture elements called *pixels*. Each pixel is a discrete numeric representation for its intensity or gray-level, that is an output coming from its two-dimensional function $f(x, y)$ fed as input by its spatial coordinates denoted with $(x, y)$ on the x-axis and y-axis, respectively [6].
A digital image can be processed by computers, this process is called *digital image processing*. It is useful to divide the mentioned process into two main categories: the methods whose output and input data are images (*image processing*) and the methods whose input data can be images and the output data are attributes extracted from the images themselves (*image analysis*).

## 1.1 General Properties

The physical meaning of the image data depends on the performed image modality. For example Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), give structural information about the anatomy of the patient. Other techniques, such as Positron Emission Tomography (PET) or Functional Magnetic Resonance Imaging (fMRI) give information about the functional properties of the patient's target organs. However, we can distinguish some general characteristics of digital images:

**Pixel depth** is the number of bits used to encode the values of each pixel and it is related to the memory space used to store the amount of the encoded information[7]. Higher the number of bits, higher the information stored but also more memory space is required[7]. A group of 8 bits is called byte and represent the smallest quantity that can be stored in the memory of a computer. For example, if an image has a pixel depth of

16 or 12 bits the computer will always store two bytes per pixel[7]. With a pixel depth of 8 bits it is possible to codify and store integer numbers between 0 and 255 ($2^8 - 1$). There are also two formats for the encoding in binary of floating-point numbers: single precision 32-bit and the double precision 64-bit.

**Pixel data** represent numerical values of the pixels are stored according to the data type. Radiological images like CT and MR store 16 bits for each pixel as integers. Image data may also be of complex type even if this data type is not common and can be bypassed by storing the real and imaginary parts as separate images. For example, complex data is provided by arrays that in MRI store acquired data before the reconstruction (the so called k-space) or after the reconstruction if you choose to save both magnitude and phase images[7].

**Metadata** are information that describe the image stored usually at the beginning of the file as a header[7]. In the case of medical images, metadata have an important role due to the nature of the images itself. For example, a magnetic resonance image will have parameters related to the pulse sequence used, timing information, number of acquisitions. More, a PET image will have information about the radiopharmaceutical injected and the weight of the patient. Medical image metadata can also include information about the patient.

### 1.1.1 Medical Image Formats

Image file formats provide a standard way to store information of an image in a computer file[8]. Medical image file formats can be divided in two categories. The first is formats intended to standardize the images generated by diagnostic modalities. The second is formats born with the aim to facilitate and strengthen post-processing analysis[7].

**DICOM** is the acronym of Digital Imaging and COmmunications in medicine. It is not only a file format but also a network communication protocol[7]. However here, we will discuss DICOM only as a medical image format.
DICOM file format establishes that the pixel data cannot be separated from the metadata[7]. In other words, metadata and pixel data are merged in a unique file. The header contains the description of the entire procedure used to generate the image in terms of acquisition protocol and scanning parameters[7]. It also contains patient information such as name, gender, age, weight, and height. For these reasons, the DICOM header is modality-dependent and varies in size. In practice, the header allows the image to be *self-descriptive*.

## 1.2 Spatial Domain Filtering

Filtering is a technique for modifying or enhancing an image. The term *spatial domain* refers to the plane of the image itself, where the related processing methods are based on the direct manipulation of the pixels. Among the various categories of spatial processing there are *intensity transformations* and *spatial filtering*. The former operate on single pixels while the latter on every pixel's neighborhood.
Mathematically, we can express this processes as follow:

$$g(x, y) = T[f(x, y)] \tag{1.1}$$

## 1.3 Segmentation

## 1.4 Radiomics

# Conclusions

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