Deep learning for online adaptive radiotherapy

Elmahdy, M.S.E.

1

Introduction

1.1 Automatic delineation in adaptive radiotherapy

Cancer is a leading cause of mortality, accounting for about 10 million deaths worldwide annually. The National Cancer Institute (NCI) predicts that by 2040, the number of new cancer cases per year will rise to 29.5 million and the number of cancer-related deaths to 16.4 million [1]. Radiotherapy (RT) is one of the widely used treatment options for cancer diseases, where a high dose of ionizing radiation damages the DNA of cancerous cells [2]. RT is frequently combined with other treatment modalities such as chemotherapy, surgery, and recently immunotherapy [3]. RT dose is usually delivered by using a technique called Intensity Modulated Photon Therapy (IMRT) or Intensity Modulated Proton Therapy (IMPT). Prior to the radiation treatment of a patient, a personalized treatment plan is constructed based on a planning CT scan and sometimes augmented with MR and/or PET images. RT doses are usually fragmented over 4 to 8 weeks resulting in 20 to 40 daily fractions [4]. Since the dose is delivered over several sessions, variations in the size and shape of the target area and Organs-At-Risk (OARs) are bound to take place. These variations are caused by multiple factors such as patient motion, weight loss, breathing, organ filling, tumors and OARs shrinkage [5]. IMPT is more sensitive to these daily changes than IMRT, which may result in the dose being distorted or dose not match the anatomy of the day [4, 6]. The simplest strategy to compensate for these variations is to account for them beforehand by adding a margin to the Clinical Target Volume (CTV) to generate the Planning Target Volume (PTV), and then generate the treatment plan using the PTV. However, these margins result in extra dose to the OARs, thus increasing the risk of toxicity, making it a suboptimal strategy. A more sophisticated approach is called Adaptive Radiotherapy (ART), where we account for inter-fraction variations by adapting the treatment plan online to the daily anatomy. Figure 1.1 illustrates

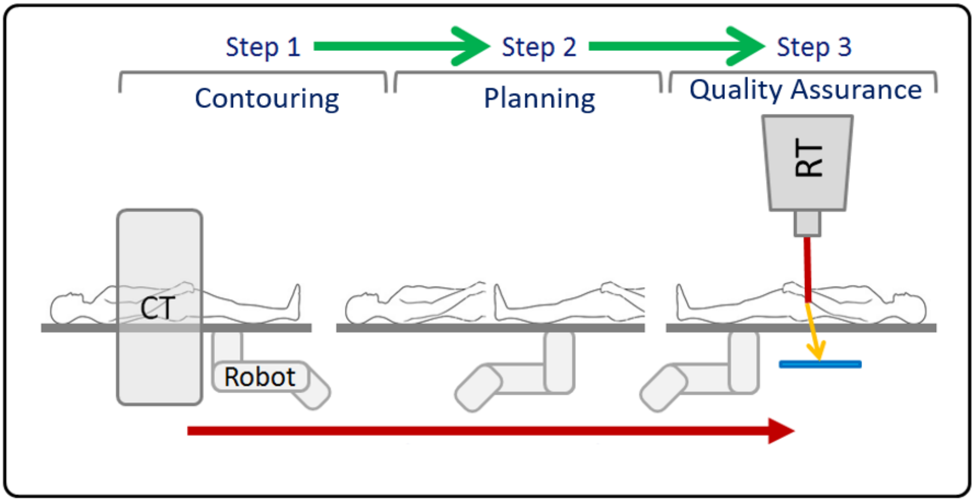

Figure 1.1: Illustration of the online adaptive radiotherapy workflow. A CT scan of the day is acquired using an in-room scanner, after which the patient table is moved to the treatment beam via a robotic arm. During the movement of the table, the daily CT scan is re-contoured and the treatment plan is adapted accordingly.

the workflow of online adaptive radiotherapy using an in-room CT scanner. However, these daily CT scans have to be delineated online to update the treatment plan. Usually this task is done by radiation oncologists according to certain guidelines [7, 8]. However, intra and inter-observer inconsistency has been noted due to preference and experience differences among radiation oncologists [9, 10]. Typically, daily manual re-contouring is not performed because it is time consuming and new anatomical variations may be introduced in the time it takes to delineate the scan [11]. Automatic re-contouring algorithms can alleviate these issues, but robust methods are required, because otherwise still time consuming fallback or correction strategies are needed. Automatic contouring can be done by direct segmentation of the daily scan, or by registration of the annotated planning scan with the daily scan followed by contour propagation. These two methods are discussed in detail in the following sections.

1.2 Image registration in radiotherapy

Image registration is the task of finding the geometrical correspondence between images that were acquired at different time steps or from different imaging modalities. In this dissertation we focus on deformable, non-linear, image registration (DIR) which accounts for local deformations such as stretching or shrinkage deformations. In the context of adaptive radiotherapy, the aim is to find the transformation that aligns the planning scan (moving image) and daily scan (fixed image) of the same

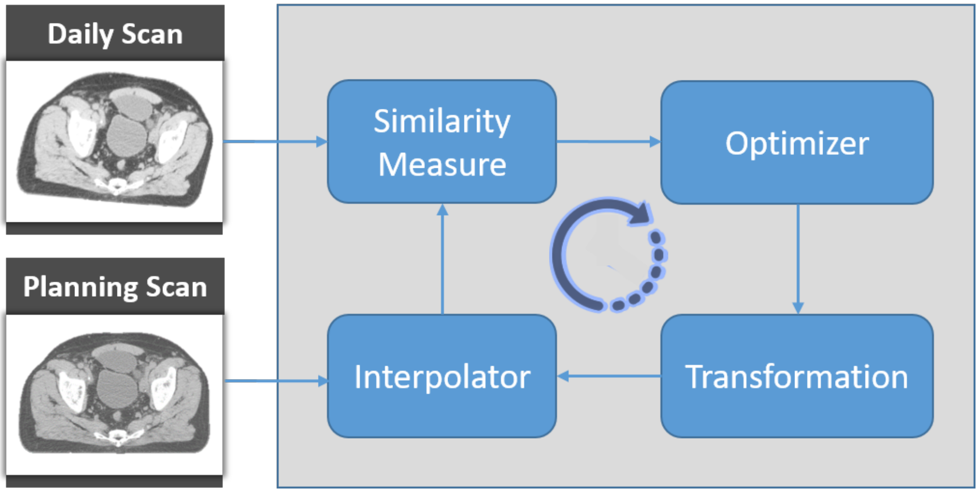

Figure 1.2: A diagram of iterative-based image registration algorithms.

patient (inter-fractional registration). DIR has been extensively integrated into RT applications such as dose planning, delivery and evaluation, since all these tasks can be improved by accounting for organ deformation. DIR is an ill-posed problem because there is no unique transformation between the fixed and moving images. Therefore it is formulated as an optimization problem (see Figure 1.2) that can be solved using iterative approaches such as Stochastic Gradient Descent (SGD):

$$\hat{\mu} = \arg\min_{\mu} C\left(I_f(\boldsymbol{x}),\, I_m(\boldsymbol{x});\, T_\mu(\boldsymbol{x})\right), \tag{1.1}$$

where $I_f(\boldsymbol{x})$, $I_m(\boldsymbol{x})$ are the fixed and moving images, C is a dissimilarity metric such as Normalized Cross Correlation (NCC), and $T(\boldsymbol{x})$ is the transformation that makes $I_m(T(\boldsymbol{x}))$ spatially aligned to $I_f(\boldsymbol{x})$. The transformation function can be modeled by a limited number of parameters (parametric transformation) or by a vector per voxel describing the displacement of this voxel in a continuous space using interpolation (non-parametric transformation). In this thesis we focus on non-parametric transformation. For contour propagation, the contour of the moving image is resampled in the fixed image domain by interpolation.

With the recent advance of deep learning, a variety of methods on learning-based registration were proposed to replace conventional iterative methods. This research either uses deep learning to model the transformation function via supervised training through synthesized deformations [12, 13, 14] or via unsupervised training by equipping the network with a spatial transformer [15] similar to the work presented in [16, 17, 18, 19]. For further details, the reader may refer to [20] where a detailed review on medical image registration using deep learning is provided.

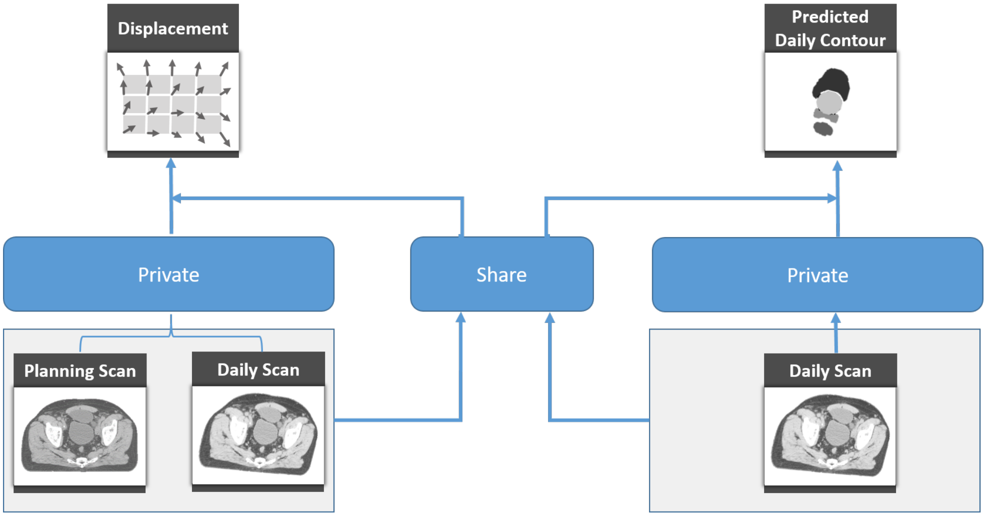

Figure 1.3: A diagram of joint registration and segmentation algorithms.

1.3 Joint registration and segmentation

Automatic contouring of the daily anatomy can be done by either a segmentation algorithm or via DIR as mentioned in Section 1.1. However, each of these tasks has its own strengths and weaknesses. For instance, image segmentation algorithms can directly delineate images based on texture and surrounding anatomy, and may therefore be robust to large organ deformations. However, it sometimes has difficulties with low contrast areas and irregularly shaped organs. On the other hand, image registration algorithms have the ability to encode prior knowledge of the patient's anatomy and therefore may perform better on low quality images. However, such methods sometimes have difficulty with large deformations. These two tasks are in fact complementary, as for example image atlases warped by image registration algorithms are often used for image segmentation [21, 22], while image contours can be used to guide the image registration method in addition to the intensity images [23, 17, 24]. Contours are also used for evaluating the quality of the registration [25, 26]. Therefore, coupling image registration and segmentation tasks and modeling them in a single framework could leverage their strengths and mitigate their weaknesses through the sharing of beneficial information. Figure 1.3 is a diagram showing how these tasks might be joined.

1.4 Accelerating MR acquisition for adaptive radiotherapy

CT-guided radiotherapy has long been the standard setup for radiation oncology despite its low contrast compared to MRI since it encodes crucial information about tissue electron density needed for dose calculation and simulation. The introduction of MRI-guided radiation therapy (MRIgRT) has revolutionized the practice of radiation oncology. This is due to the superior performance of MR images over CT in terms of soft tissue contrast (see Figure 1.4), which facilitates the monitoring of the daily anatomical changes and subsequently adapt the treatment radiation in real-time. Any substantial latency in this MRI-guided workflow might, however, result in the introduction of new anatomical variations and subsequently the delivered dose would be different from the intended dose [27]. One of the potential causes for this latency is imaging latency, which represents the time delay between the anatomical change and its emergence in the reconstructed image.

Therefore, fast image acquisition and reconstruction are crucial to improve the performance of current MR scanners, which led in recent years to the development of techniques such as parallel reception, compressed sensing and multi-band accelerations. However, there is still a need for further scan acceleration. The long acquisition time is intrinsic to the scanner and physics properties of MRI. For the majority of scans performed in clinical practice, this acquisition is done through consecutive read-outs of single lines in k-space. The scanning time could be shortened by reducing the number of acquired lines in k-space, i.e. by undersampling the 2D or 3D k-space. However, this could violate the Nyquist criterion, resulting in aliasing and blurriness in the reconstructed images. These issues may result in a lag between the organ positions derived from the reconstructed image and the actual positions by the time the acquisition is finished. Compressed Sensing (CS) is one of the most common solutions for acceleration by undersampling, while maintaining image quality. CS was introduced by Donoho [28], Lustig [29] and Candes [30], where it leverages the fact that MR images can be compressed in some domain, restoring the missing k-space data through an iterative reconstruction algorithm [31].

Recently deep learning-based algorithms were introduced in order to reconstruct a high quality MR images at acceptable speed. These algorithms often focus on modeling iterative approaches similar to CS algorithm via deep learning models [32, 33, 34].

1.5 Outline of the thesis

The aim of the work described in this thesis is to develop a deep learning-based methodology for automatic contouring for real time adaptive radiotherapy either guided by CT or MR imaging modalities. Our proposed automatic contouring networks were trained and tested on CT images since it is the commonly used for treatment planning, while for MR we focused on the other bottleneck, i.e. the reconstruction time.

Chapter 2 presents a contour propagation pipeline that combines conventional iterative-based registration with a deep learning model. We propose a CNN network

Figure 1.4: Example of prostate images, where from left to right are CT, T2-weighted MR, and fat suppressed MR images [35].

that automatically segments the bladder, and then feeds it to the registration algorithm as prior knowledge of the underlying anatomy. We also introduce a GAN model to address the problem of gas pockets in the rectum to avoid the registration algorithm to be distracted.

Chapter 3 presents a novel transfer learning approach in order to leverage personalized anatomical knowledge accumulated over the treatment sessions. We adapt a baseline segmentation model as the patient goes through their RT treatment. Thus, instead of depending on a static deep learning segmentation model for all patients, we accumulate knowledge over successive sessions for a particular patient. This accumulated knowledge is then used to encourage the model into predicting a segmentation that has a higher quality for this specific patient.

Chapter 4 proposes to combine the registration and segmentation tasks in a deep learning setting using adversarial learning. The proposed framework consists of an unsupervised 3D end-to-end generator network that estimates the deformation vector field (DVF) between the input image pairs. Meanwhile, a discriminator network is trained to evaluate how well the registration is performing.

Chapter 5 proposes to formulate the registration and segmentation as a joint problem via a Multi-Task Learning (MTL) setting, allowing these tasks to leverage their strengths and mitigate their weaknesses through the sharing of beneficial information. We explored different joint network architectures as well as loss weighting methods for merging these tasks, thus pinpointing the best strategy to maximize the information flow between the two tasks.

Chapter 6 presents a fast MR reconstruction algorithm, which enables the application of the automatic contouring methods proposed in the previous chapters for online adaptive MR-guided radiotherapy. Starting from undersampled k-space data, an iterative learning-based reconstruction scheme inspired by compressed sensing theory is used to reconstruct the images. We developed a novel deep neural network to refine and correct prior reconstruction assumptions given the training data. The proposed network was ranked #1, shared #1, and #3 on respectively the 8x accelerated multi-coil, the 4x multi-coil, and the 4x single-coil tracks in the fastMRI competition organized by Facebook and New York University (NYU).

Chapter 7 summarizes and discusses the ideas presented in this thesis.