

Novel MR techniques in rectal cancer

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Chapter 9

Valorisation

In the last century, significant steps have been made in the treatment of cancer. Although there is no therapy to cure every type of cancer, in many types of cancer treatment strategies have evolved to make it a chronic illness that can be managed and controlled for a long period of time. Despite these developments, cancer is still in the top 10 of causes of death in the Western World. Colorectal cancer in specific is the 3rd and 2nd most common type of cancer in men and women, respectively and worldwide the 3rd most common cause of cancer death. Rectal cancer accounts for approximately one third of all colorectal cancers, with 500 new cancer diagnoses in the Netherlands every year. Patients with rectal cancer traditionally had a very poor prognosis, mainly due to the high risk of a local recurrence of the tumour after surgery. The introduction of standardised surgical techniques (total mesorectal excision), as well as neoadjuvant treatment (chemotherapy and radiation therapy) for patients with more advanced tumours have lowered the number of local recurrences drastically. These discoveries further stimulated the urge to personalize treatment for each individual patient. To decide which patient benefits from which treatment it is important to divide the patients in different risk categories based on their primary tumour status. There are three main risk categories: low risk tumours that can be treated with direct surgery without neoadjuvant treatment, intermediate risk tumours who receive a short course of radiotherapy before surgery, and the high risk group with locally advanced tumours who receive a long course of neoadjuvant chemoradiotherapy (CRT) to downstage the tumour before surgery. MRI plays a key role to stage rectal tumours in order to determine the tumour risk profile and thus the appropriate treatment for each individual patient. Recently there have been new developments to further personalize treatment in rectal cancer, the most important one being the introduction of 'organ saving' treatment strategies. Up until recently all patients with advanced rectal tumours treated with neoadjuvant chemoradiotherapy proceeded to surgery, regardless of the response to the chemoradiotherapy. In a small percentage ($\pm 15\%$) of these patients, the response to chemoradiotherapy is so substantial that no residual viable tumour is found at surgical resection. For these patients it may now be considered to defer from radical surgery and instead monitor the patients ('wait-and-see') or perform a small local excision, thereby saving the rectum and preventing a stoma and other peri- and postoperative morbidity. In the light of these organ-saving treatments, it becomes more and more important to accurately evaluate the response to chemoradiotherapy with imaging or even predict before the start of treatment which patients are likely to show a good response to chemoradiotherapy so that the neoadjuvant treatment may be further optimized. Standard morphological MRI will no longer be sufficient to answer these more advanced

imaging questions and new techniques will need to be developed and studied to meet the new clinical needs.

One of the most important new techniques that has been developed and studied for rectal cancer imaging in recent years is diffusion-weighted imaging (DWI). DWI is a type of MR sequence that can easily be added to any routine rectal MRI protocol. It can provide radiologists with unique information on the cellularity of tissues and has shown great benefit for the differentiation between high-cellular (tumour) and non-cellular (non-tumour) tissues. At the start of this thesis, the use of DWI had mainly been studied in purely research settings and studies focussing on implementation of DWI in clinical settings were lacking. Moreover, previously studied methods of DWI analysis so far often included quantitative measurement methods that are impractical and time-consuming and therefore difficult to implement in daily practice. This triggered us to study practical ways to use DWI in a clinical setting, and to make it available and applicable for every radiologist, to avoid that this potentially promising and potentially clinically beneficial technique may get stuck in research settings. Therefore, the main aim of this thesis was to look for strategies and tools that can benefit the clinical use of DWI in different clinically relevant scenarios within the spectrum of rectal cancer treatment.

RELEVANCE OF SCIENTIFIC RESULTS IN THIS THESIS

The results of the thesis offer several practical points of advice on how DWI may be used for rectal cancer management. First, it shows that after a certain training every radiologist can use DWI for tumour response assessment after neoadjuvant treatment, with results similar to those previously reported for expert readers in research settings. Moreover, we also discovered several important pitfalls and learning points, that can serve as a teaching reference for future radiologists. Second, this thesis shows that DWI can very practically be put to use to help select patients with a complete response of their lymph node metastases after chemoradiotherapy by simply counting the number of lymph nodes on DWI, a method that is easily applicable for daily use. Finally this thesis shows different ways in which quantitative analysis of DWI can be performed in a more practical manner. The use of DWI tumour volumetry has previously been shown to be promising. However due to the time-consuming nature of manual delineation of tumour volumes it has not yet found its way to clinical practice. This thesis shows that there are other ways to measure tumour volumes on DWI that are easier, quicker and offer similar results. Based on the results of this thesis, the use of more advanced quantification methods at this point has no clear added value for clinical use.

TARGET POPULATION

All patients with rectal tumours routinely undergo MRI as part of the clinical diagnostic path, according to the national guidelines. Patients with intermediate or high risk tumours then receive neoadjuvant treatment, followed by surgery (or in some cases by organ-saving treatments, as discussed above). These patients undergo a second restaging MRI to assess the tumour response. The target population includes all these patients undergoing MRI. In addition, the radiologists who assess the MR Images are part of the target population of this thesis, as the teaching of radiologists is a very important feature that will benefit the actual use of novel MR techniques and its implementation in clinical protocols.

INNOVATION AND FUTURE

The role of imaging in the treatment of cancer has grown considerably with ongoing developments in cancer treatment. Introduction of novel imaging strategies such as the use of diffusion-weighted MR imaging in rectal cancer can facilitate the selection of patients for organ-saving treatments. However, there is no clear consensus on the best strategy to put DWI to use in daily practice. Although the results of these thesis already contribute to solving this issues, further research is still required, particularly with respect to quantitative DWI evaluation. An important next step is multicenter validation of (semi-)automated DWI volumetry methods

Moreover, the same path to translate research into daily practice should be explored for other novel imaging techniques apart from DWI (which was the main focus of the current thesis), for example perfusion and fibrosis imaging. Ultimately, the future most probably lies in finding a way to smartly combine these different techniques. Such multiparametric imaging evaluations most likely will offer the most comprehensive insights into tumour biology and can be expected to contribute a better understanding of cancer and treatment processes and thereby ultimately help to further personalize and optimize treatment individual cancer patients.