Multimodality and multi-parametric imaging in abdominal oncology

ON THE IMPACT OF THIS THESIS

Main aims and outcomes of this thesis

The overall aim of this thesis was to investigate how combined use of different medical imaging modalities, in specific the combination of magnetic resonance imaging (MRI) and positron emission tomography (PET), can benefit the diagnostic assessment and treatment of patients with cancer that originates from one of the abdominal organs. To investigate this, we formulated three main research questions, that together compose the different chapters of this thesis:

1. What can we learn from published literature?
2. How can we benefit from the combination of PET and MRI when visually interpreting these images to diagnose and determine the cancer stage in patients with abdominal cancers?
3. Are quantitative measurements derived from the tumour on PET and MRI useful as "markers" to help predict how well patients with abdominal cancers will respond to their anti-cancer treatment?

From our literature search described in Chapter 2 we have learned that during the last decade there has been a tremendous increase in published research involving multimodality cominations of PET(/CT) and MRI, not in the least part due to introduction of hybrid PET/MRI scanners. Hybrid PET/MRI refers to the combined acquisition of PET and MRI images using a single machine. The clinical introduction of these machines as of 2011 has greatly boosted PET/MRI research, though the clinical role and added value of hybrid PET/MRI remains to be established. Another important development has been the increase in use of new PET tracers, with the ability to more specifically target certain tumour types, such as prostate cancer or neuroendocrine tumours. Finally, we have learned that in addition to combined use of PET(/CT) and MRI for visual diagnostic evaluations, there is a rapidly growing interest for more advanced quantitative analysis of the images. We have investigated this quantitative approach ourselves in Chapters 4-6, but first performed a study with cases from our own institution to determine the benefit of combined visual assessment of PET and MRI for diagnostic staging. In Chapter 3 we reviewed 201 patients who underwent a combination of PET/CT and MRI as part of the same diagnostic staging workup. The combined imaging sets were re-assessed by a nuclear medicine physician and a radiologist together as a team, and their combined imaging findings were compared to the reports of the original, separate assessments to establish how this combined

assessment might have impacted diagnosis and treatment. We learned that integrated (side-by-side) evaluation of the images had a small positive effect on the confidence with which the diagnosticians could reach a uniform diagnosis, with a potential impact on treatment planning in approximately 1 out of 9 patients. Finally, in the last three chapters we focused on the value of "quantitative" assessment of PET and MRI data in patients with rectal cancer (Chapter 4), cervical cancer (Chapter 5) and anal cancer (Chapter 6). Quantitative imaging refers to an approach where measurable variables are extracted from the images, varying from simple measurements, such as tumour size or volume, to more specific parameters, such as the 'maximum standardized uptake value' (SUVmax) which describes the glucose uptake on PET, or 'texture' measurements that describe the spatial heterogeneity of tumour signal within an image. In chapters 4-6 we combined these variables, derived from PET and MRI scans performed before the start of treatment, with other more clinical variables such as patient age, sex and overall disease (TNM) stage, to build statistical models to predict the chance of a successful treatment outcome. We learned that, though some of these parameters – such as tumour volume, signal heterogeneity and SUV – had some predictive value, it were parameters derived from visual assessment of the images (e.g. tumour and nodal disease stage) that were valuable in the prediction of patient outcomes. This stresses the need for a good quality visual diagnostic assessment of medical imaging by experienced diagnosticians.

Relevance of this research

With this thesis we have shown that integration of PET and MRI in diagnostic workflows – via hybrid acquisition and/or integrated assessment by dedicated diagnosticians – can contribute to improved reader confidence and a reduction of inconclusive or conflicting diagnostic outcomes, thereby potentially changing clinical management in a substantial number of patients with abdominal cancer. This suggests that adopting such integrated workflows into clinical practice can have a positive clinical impact, urging the need for further collaboration and integration of Radiology and Nuclear Medicine departments. Whether hybrid PET/MRI acquisition will eventually become widely accessible, if it should replace the "stand-alone" combination of MRI and PET/CT, and for which particular diagnostic indications, remain major questions to be addressed by future research. Finally, we have shown that clinical prediction models incorporating information derived from imaging via visual assessment and (to a lesser extent) quantitative measurements, can aid in predicting the outcome of anti-cancer treatments – though further studies are obviously needed. Considering that these treatments are often costly and associated with (long-term) morbidity or

disability, selecting the right patient for the right treatment based on the anticipated treatment effect is highly relevant to improve patient outcomes and more effective use of healthcare resources.

Target population

There are several audiences that may benefit from the research presented in this thesis. Firstly, our findings on the evolution of multimodality PET(/CT) and MRI imaging in the literature will be of interest to radiologists and nuclear medicine physicians, as it provides valuable insights into recent developments in their workfield, and indicates likely courses for the (near) future. Our study on integrated PET/CT and MRI assessment will be of interest to the same groups, particularly those leading or working in departments where integrated reporting is currently not (yet) the norm. Our results may provide insight into what benefits can be expected, and on how to implement and evaluate the effects. Second, researchers conducting studies on response prediction or descision support models may benefit from the results of the studies presented in **Chapter 4-6**. They can compare these to their own findings, or consider using a similar strategy or method to design their own studies. Finally, the findings and recommendations formulated in this thesis could inspire further research in the proposed directions, hopefully to the benefit of more expedient use of imaging and treatment, to ultimately benefit the quality of healthcare and patient outcomes.

Activities

The research presented in this thesis has been shared actively within the research community by publication in peer-reviewed journals and by presentation at multiple national and international conferences. The projects that were conducted and the presented results have contributed to the formation of a 'hybrid imaging team' at the Netherlands Cancer Institute, boosting the collaboration between the Radiology and Nuclear Medicine department in research and diagnostic reporting. Finally, our work on quantitative imaging analysis has been continued as part of an ongoing multicenter project on multiparametric imaging modelling in rectal cancer.