Mri-Based Radiomics in Breast Cancer

Impact paragraph

Main findings

This thesis investigated the use of MRI-based radiomics to advance personalized breast cancer care. First, the current knowledge was assessed through a systematic review, followed by the development of models to predict axillary lymph node metastases and pathologic complete tumor response to neoadjuvant systemic therapy. Both studies concluded that radiomics models based on MRI exams have not (yet) contributed to these predictions. However, these studies did not consider the effect of different acquisition and reconstruction parameters and the use of different MRI scanners on the extracted radiomic features, as this data was not available at the time. The estimate that these parameters affect the radiomic features is based on studies in CT imaging that showed that many radiomic features were sensitive to these effects. These studies concluded that this should be corrected before performing radiomics analysis.

In the second part of this thesis, we consequently focused on the optimization of MRI-based radiomics. One study looked at the stability of features with respect to inter-rater segmentation variability. Since automatic tumor segmentation in breast MRI is not yet sufficiently developed, studies are still dependent on manual or semi-automated tumor segmentation. For two commonly used radiomics software packages, features were identified that proved robust to manual tumor segmentation. In the MRI test-retest study, we identified a limited number of features that were repeatable regardless of the test-retest setting and scanning date for MR images used in a clinical breast protocol. These repeatable features can be used as a starting point to investigate feature reproducibility, the next step towards obtaining generalizable and comparable MRI-based radiomics results.

Relevance

Worldwide, breast cancer is the most common cancer in 2020 with 2.26 million new cases. In the same year, breast cancer ranked fifth place of most common causes of cancer death with 685,000 deaths. Breast cancer is also the most common form of cancer in the Netherlands, with each year, approximately 17,000 new breast cancer diagnoses (2). Progress in the treatment of breast cancer patients, therefore, has a major impact. Its treatment consists of surgery, systemic therapy (consisting of hormonal therapy, chemotherapy, and immunotherapy), and radiotherapy. Breast cancer is a heterogeneous disease with many variations in (non)-genetic characteristics. These variations require different treatments, ideally tailored to the individual breast cancer patient. Treatments tailored to the individual patient are called personalized medicine and have already resulted in significant progress in the treatment of breast cancer.

To advance personalized medicine, multiple sources and tools are used today, of which one is radiomics. Radiomics translates routine medical images into quantitative data that can serve as a biomarker for use in clinical decision support systems. In recent years there has been a huge increase in radiomics research, and despite mainly positive published results, incorporation of radiomics in clinical decision support systems is lagging. This is caused by various factors, including feature sensitivity to differences in acquisition and reconstruction parameters. In this thesis, the lack of this data most likely resulted in radiomics and combined models that did not contribute to the prediction of tumor response to neoadjuvant systemic therapy and radiomics and models that did not contribute to the prediction of axillary lymph node metastases.

Specifically, for breast MRI, it was even unknown whether features would remain stable when extracted from multiple scans of the same patient, scanned on the same MRI scanner with identical acquisition and reconstruction parameters. The performed MRI test-retest study gave answers to that and showed that, in the specific breast MRI setting, only a small part of the extracted features was repeatable. Most likely, further research on breast MRI-based radiomics should focus on this subset of features and examine their reproducibility. Based on this data, and after assessing feature reproducibility, radiomics analysis can be performed more reliably.

In addition, breast MRI tumor segmentation was investigated, segmentation is a necessary step before radiomics analysis can be performed. In this thesis, we identified a subset of features being robust to variability in manual tumor segmentation. As long as manual or semi-automatic segmentation is performed in breast MRI-based radiomics studies, this information can be included as a feature selection procedure.

Target population

The findings of this thesis are relevant for a broad target group; ranging from the radiomics community, technology companies and software developers, radiologists, and breast cancer patients.

- In general, reproducibility of radiomic features and the generalizability of radiomics results are issues that generate a significant amount of debate in, not limited to, the radiomics community. For that reason, many recently published radiomics articles focus on these topics and it is often concluded that reproducibility studies should be part of the data analysis itself, as it appears to be tumor site-specific. However, most of these articles use CT imaging. MR images are even more challenging since they lack the standard grayscale intensities like the Hounsfield units in CT. No test-retest study specific to breast MRI has yet been conducted, so the results of this repeatability study are a starting point for any scientist in this research field to further analyze feature reproducibility in MRI. Furthermore, this research strategy can be a source of inspiration for researchers who are investigating other tumor areas using MRI.
- The results described in this thesis may also be of interest to technology companies and their software developers, given the high reliance on software in the use of radiomics. On the one hand, for writing automatic breast MRI segmentation software, because many features were not reproducible with the still widely used manual segmentations. On the other hand, for optimizing the open-source radiomics feature extraction software, where transparency should be paramount to obtain generalizable and reproducible results.
- Although the results of this thesis are especially interesting for the scientist working in this field, it is also important that the radiologist is aware of the results of this thesis. It is ultimately the radiologist who will be using radiomics in the clinic, so it is good to involve this department in the research process early on. This also ensures that they themselves can contribute to the purpose of radiomics; assisting and supplementing the radiologist’s work through clinical decision support systems.
- Ultimately, it should be the breast cancer patient who benefits from all the radiomics-related research. Although implementation in the clinic still seems a long way off, clear goals will drive progress. The application of MRI-based radiomics is likely to be first used in breast cancer diagnosis. The greatest impact on breast cancer treatment is likely to occur if the accurate prediction of tumor response becomes possible. If pathologic complete response can be predicted accurately prior to surgery, surgery and/or adjuvant therapy can potentially be omitted. In contrast, breast cancer patients who do not respond to neoadjuvant therapy can be operated on immediately.

Activities / Implementation

The results of this thesis were published in renowned international journals. Although some of them are mainly focused on the technical side of radiomics, it was decided not to publish mainly in technical journals because we think it is important that the clinician for whom radiomics will be useful in the future is already aware of the current developments. In addition, the results were presented at both national and international conferences, raising awareness among scientists working in the radiomics field, as well as clinicians working with breast cancer patients. It is especially important that radiologists, who will probably be the first users in the clinic, are involved in the development of MRI-based radiomics at an early stage so that they can also think along the implementation process. It is therefore a positive sign that the (inter)national radiological conferences are increasingly focusing on artificial intelligence, including radiomics. Furthermore, presenting our latest work in future radiomics conferences or courses like *Artificial Intelligence 4 Imaging* is an ideal way of disseminating the results to a community of leaders in the field.