Advances in MRI of the colon and pelvic floor
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Chapter 9

Summary, conclusions and implications
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Summary

Part 1: MRI of the colon

In the first part of this thesis we addressed certain aspects of magnetic resonance (MR) colonography, which comprises a method permitting the evaluation of the colon for disorders. Chapter 2 comprises an overview of the current status of MR colonography in the literature regarding examination indications, image interpretation, applied bowel preparation methods and results of diagnostic accuracy.

In chapter 3 our objective was to determine accuracy estimates of MR colonography for the detection of colorectal lesions. Also, methodological quality and accuracy of reporting was assessed for proposing future reporting recommendations in this field. Therefore, the available literature of prospective primary studies which have compared the diagnostic accuracy of 1.5T or 3.0T MR colonography to completed colonoscopy in detecting colorectal lesions was systematically reviewed and a meta-analysis was performed. Thirteen studies were included, evaluating 1285 patients with a mean disease prevalence of 44%. The included studies were difficult to compare due to little uniformity in essential study design characteristics, which precluded a meta-analysis of polyp detection for all different size thresholds. We were only able to perform a meta analysis for polyps 10 mm and larger for which the per-patient summary sensitivity and specificity estimates were 88% and 99%, respectively. Therefore, it seems reasonable to assume that MR colonography can play a role in the detection of large colorectal polyps in patients at increased risk of CRC. Based on the considerable heterogeneity in data reporting we encountered during this systematic review, a more standardized reporting is needed in future diagnostic studies on MR colonography.

CT colonography research has documented a wide inter-observer variability in polyp detection between radiologists. Accordingly, diagnostic accuracy is considered to be largely determined by observer performance and double-read strategies might improve sensitivity in CT colonography. Current MR colonography protocols result in a relatively large number of series to be interpreted when compared to CT colonography, potentially leading to reader fatigue and ultimately influences reader performance. In order to explore the role of non-radiologists as potential observers for double-read purposes, we sought to determine if non-radiologists were able to interpret intraluminal findings in MR colonography. In chapter 4, MR colonography of 159 patients at increased risk of colorectal cancer were independently assessed by two trained radiographers and
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the performance characteristics were compared to those of two trained radiologists in the detection of colorectal polyps. Our data showed no significant differences in detection rates for polyps 10 mm and larger. However combined specificity differed significantly between radiologists and radiographers (96% and 73%, respectively). Although the combined sensitivity rates suggest a comparable diagnostic performance of both the radiologists and radiographers, prior colonography and MRI experience favoured diagnostic outcomes with regard to specificity. Currently no added diagnostic value is to be expected of non-radiologists as potential observers for double-read purposes. More research will have to be performed on the required level of expertise for reading MR colonography since diagnostic accuracy was principally impeded by an inaccuracy in interpretation rather than a technical limitation in visualizing colorectal polyps.

Conventionally, colonic distension in MR colonography literature is mostly achieved by the use of a water enema. In chapter 5 we evaluated the feasibility of using automated insufflation of carbon-dioxide ($CO_2$) for luminal distension at 3.0T MR colonography in fourteen healthy subjects. Furthermore, four different bowel preparation strategies were compared in terms of image quality and burden. Overall, automated $CO_2$ delivery resulted in an adequate to optimal distension of the colonic segments and was not associated with susceptibility artefacts at air / tissue interfaces. Despite of the usage of a spasmolytic agent, in the fast gradient echo series image quality was influenced by (bowel) motion artefacts, which impeded diagnostic confidence. The type of applied bowel preparation principally determined the overall experienced burden during the MR colonography examination in all four strategies. Although we demonstrated technical feasibility of automated insufflation of $CO_2$ as luminal distending agent, minimizing bowel motion artefacts is essential to make this technique appropriate for prospective clinical studies.

Part II: MRI of the pelvic floor
The second part of this thesis focused on the radiological evaluation of the female pelvic floor using different types of MRI techniques to describe the functional pelvic floor support.

In chapter 6 we assessed the reliability of prolapse staging using dynamic MRI by three differently skilled observers and we compared prolapse stages as assessed on dynamic MRI with a standardized method of clinical prolapse staging (i.e. Pelvic Organ Prolapse Quantification (POP-Q)). In addition we evaluated whether radiological prolapse staging and prolapse staging by physical
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examination correlates with manifest pelvic floor symptoms. Therefore, we compared three different groups which consisted of ten patients with pelvic floor symptoms and at least stage 2 prolapse, ten patients with pelvic floor symptoms but prolapse stage 1 or less and ten nulliparous women without pelvic organ prolapse or pelvic floor symptoms. Four predefined reference lines were used for radiological determination of a prolapse (i.e. pubo-coccygeal line (PCL), mid-pubic line (MPL), perineal line and the H-line). We found good to excellent intra-class correlation coefficients between the observers in the anterior and middle compartment, for all applied reference lines. Correlation between MRI and clinical findings were most pronounced in the prolapsed group, but not for all reference lines. In addition the correlation of MRI-based staging and POP-Q with pelvic floor symptoms was non-satisfactory.

Diffusion tensor imaging (DTI) encompasses a distinctive non-invasive method to describe the directionality of the internal microstructure within anisotropic tissues, and its application has been used to visualize and characterise brain white matter tracts and skeletal muscle. In chapter 7, we evaluated the feasibility of visualising the normal pelvic floor musculature in five healthy female nulliparous subjects using 3.0T DTI and fibre tractography. In addition, estimates for basic DTI measures (mean eigenvalues ($\lambda_1, \lambda_2, \lambda_3$), fractional anisotropy (FA) and mean diffusivity (MD)) were recorded for isolated muscles. Fibre tractography resulted in an acceptable representation of muscle morphology and fibre orientation of the pubovisceral muscle, perineal body, anal - and urethral sphincter complex and internal obturator muscle in all female subjects. Also, we established a range of anisotropic measures with overall small standard deviations for clinically relevant anatomical structures in the pelvic floor. Therefore, we concluded that DTI with fibre tractography enables the three-dimensional (3D) visualization of the normal female pelvic support.

In exploring the potential clinical applications of diffusion tensor imaging (DTI) and fibre-tractography of the pelvic floor support, our initial hypothesis in chapter 8 was to demonstrate differences in basic DTI parameters (MD, FA) in the female pelvic floor support in healthy and pathological conditions. Therefore we included three groups of women, consisting of women with pelvic floor symptoms and clinically significant pelvic organ prolapse; women with pelvic floor symptoms but without clinical relevant pelvic organ prolapse and nulliparous women, without pelvic floor related symptoms nor pelvic organ prolapse (same groups as in chapter 6). Fibre-tractography permitted both quantification and comparison of basic DTI-parameters of the anal sphincter

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complex, perineal body, the puboperineal muscle - a subdivision of the pubovisceral muscle - and the internal obturator muscle among the three groups and our data showed substantial inter-observer agreement in determine basic DTI parameters of these four anatomical structures. Still, we were able to track only part of the initially defined anatomical structures and from tracked structures no statistical significant differences were found among the three groups. Since tractability and non-tractability of pelvic floor structures proved equally distributed among the three groups in this study, technical limitations as clarification of the limited tractability is presumed rather than morphological alterations of the pelvic floor support. Yet, the fact that fibre tractography was only satisfactory achievable for a relatively small quantity of structures, limits the application of this technique for the moment.

Conclusions

Chapter 3. MR colonography can accurately detect large polyps and masses, yet large clinical trials evaluating MR colonography accuracy are lacking.

Chapter 4. Radiographers can perform comparably to radiologists in detecting large polyps at MR colonography, but an added benefit of double-read is not to be expected.

Chapter 5. Using automated carbon dioxide (CO₂) delivery for colonic distension in 3.0T MR colonography is practicable.

Chapter 6. Dynamic MRI in prolapse staging is consistent but has an insufficient correlation with both POP-Q findings and clinical symptoms.

Chapter 7. 3.0T DTI with fibre tractography permits the three-dimensional visualisation of the normal female pelvic support.

Chapter 8. 3.0T DTI with fibre tractography of the female pelvic support has fairly strong inter-observer agreement but does not identify muscle injury.

Implications

To date, colonoscopy is considered the diagnostic standard to examine the colorectum. For less invasive colorectal evaluation, a number of radiologic imaging examinations have evolved of which CT colonography has proved to provide a similar yield as colonoscopy for colorectal cancer and large polyps. For MR colonography we can conclude that the sensitivity for detection of large
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colorectal polyps and colorectal masses is approaching that of CT colonography, and therefore might play a role in the detection of large colorectal polyps. However importantly, MR colonography has not progressed significantly since its introduction with still mediocre results for medium sized lesions and certainly lacks large prospective diagnostic studies. Thereby, there is no broadly accepted, uniform technique. Further, there is a considerable heterogeneity in MR colonography data reporting and therefore the MR colonography research community should adopt similar reporting recommendations to those of CT colonography as far as applicable. In this respect standardised per-patient and per-polyp data presentation and a minimum data set for study level reporting are most essential.

Also, description of observer experience in MR colonography should be refined in MR colonography study reporting. So far, the required level of experience to reach a satisfactory accuracy is not known and has never been evaluated in MR colonography. Moderate diagnostic accuracy as found in our study, was predominantly due to errors in the detection of colorectal abnormalities at MR colonography (lesions were often identified in retrospect), underlining the importance to define both the desired level of expertise and the type of training program. Factors negatively influencing interpretation of MR colonography images include the relatively large number of series that must be read for each data set (which ultimately provokes reader fatigue), and the effects of a relatively wide slice thickness, leading to less reliable identification of especially smaller lesions. Enhancing sensitivity of MR colonography using a double-read strategy with non-radiologists as second readers, does not seem useful. In view of the complexity of MRI interpretation, the actual number of validated cases for training purposes presumably will be substantially higher in MR colonography than in CT colonography and must be established in prospective further research.

Improving accuracy of MR colonography among others includes using state of the art techniques into the current MR colonography scan protocols. High-field abdominal imaging allows for isotropic high spatial resolution and thus the ability to reconstruct acquired 3D data stacks in different orthogonal planes (MPR), consequently resulting in a reduction in number of series to be acquired. The introduction of automated CO₂ insufflation for luminal distension in MR colonography resulted in an adequate colonic distension, and thereby avoids the need of an water-based enema in the MRI suite which is regarded as the most burdensome element of a MR colonography examination. However further prospective clinical studies are necessary to determine the precise diagnostic
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performance and acceptance of this technique in MR colonography and must include the addition of intravenous gadolinium contrast medium to increase contrast-to-noise ratios (CNR) between bowel wall and bowel lumen.

In conclusion, the limited availability, higher costs, time, complexity and inferior evidence regarding its role in the detection of medium-sized polyps, are still disadvantages of MR colonography over CT colonography in daily practise. However, continuous technical progress and increasing availability of higher magnetic field-strength MR units allows better image quality and might ultimately lead to an improved accuracy in the evaluation of the colon. Together with new developments, i.e. the implementation of diffusion weighted imaging (DWI), MR lymphography and molecular imaging, MRI of the colon may gain a role in the radiological evaluation of patients at risk for CRC in the near future. In particular upcoming developments of using the versatility of MRI to image cellular and molecular processes, e.g. targeted imaging in colorectal cancer screening, should be studied.

To date, pelvic floor disorders are only partly understood, which is emphasized by the poor correlation between anatomical and functional abnormalities of the pelvic floor. Towards an improved understanding of mechanisms leading to pelvic organ prolapse, a diversity of imaging techniques have been proposed in pelvic floor imaging. With regard to dynamic MR imaging of the pelvic floor, we found an insufficient correlation of dynamic MR imaging with both clinical examination (POP-Q) and symptoms of pelvic organ dysfunction. This is in line with previous studies in this field. Therefore one can question whether dynamic MRI of the pelvic floor provides extra diagnostic information in clinical-decision taking in pelvic organ prolapse. Developments in dynamic imaging of the pelvic floor support in an upright position using open-magnet MR units, thereby simulating normal physiological conditions, might add value to existing protocols. However, given the almost complete lack of such magnets worldwide, this is not a practical solution for this moment.

By introducing DTI in pelvic floor imaging we aimed to describe the pelvic floor integrity using a technique which exceeds the resolution of conventional MR techniques, and was not previously proposed in pelvic floor imaging. Initial feasibility of visualizing the healthy pelvic floor support allowed to study the potential role of DTI in demonstrating alterations in the pelvic organ support in pelvic floor dysfunction. Yet, in our cross-sectional study the power was most likely insufficient to reveal pelvic floor abnormalities and in addition tractography
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was attainable in part of the pelvic floor support, ultimately limiting the application of this technique for the moment. In our point of view, DTI and tractography of the pelvic floor does not yet have the ability to be implemented as a diagnostic test on an individual level, among others due to large per-subject variation in tissue characteristics. However, we reported the initial experience and it might be regarded as an evolving non-invasive pre-clinical research tool which is able to provide new insights in pelvic floor abnormalities in the search for possible etiologic factors of pelvic floor dysfunction. We feel that future research should focus on optimizing spatial resolution, to visualize anatomical structures which were currently insufficiently identified, without significant loss of SNR which would ultimately decrease DTI accuracy. Additionally, continuing developments of using high angular resolution diffusion imaging (HARDI) gives new possibilities to enhance DTI of the female pelvic floor.