Diagnostic value of novel MR imaging techniques for the primary staging and restaging of rectal cancer

This trial was only completed in part, because the contrast agent that was being used for the study (gadofosveset trisodium) was no longer commercially available. As such, two of the main study outcomes related to lymph node staging and perfusion imaging (for which administration of the contrast agent would be required) could not or only partly be analyzed.

A summary of the (preliminary) outcomes of this study is provided below. A list of published abstracts and manuscripts related to data acquired as part of this trial is provided at the bottom of this document:

Tumor response evaluation with diffusion-weighted MRI (DWI):

Compared to the use of standard MRI, the addition of diffusion-MRI led to an improvement in the diagnostic confidence of radiologists in determining the final tumor stage after chemoradiotherapy. After addition of DWI the number of uncertain ('equivocal") scores to discriminate between a complete response and residual tumour decreased from a maximum of 16% to 7-12%. For non-expert radiologists, no significant improvement in diagnostic accuracy was observed after the addition of DWI. For expert radiologists, diagnostic accuracy improved from 80% to 83%. In general the expert radiologists achieved a better diagnostic performance compared to non-expert readers (80-83% versus 73-79%).

For discriminating between a complete response and residual tumour the addition of diffusion-MRI to the standard MRI protocol led to an upstaging in 6.7% of the cases for expert radiologists and 7.4% for non-expert radiologists; conversely it led to a tumour downstaging in 6.7% and 11.1% respectively. To assess the extent of residual tumour (yT1-2 versus yT3-4 residual tumour) the addition of DWI led to an upstaging in 1.4% and 0% (expert and non-expert) and a downstaging in 12.1% and 6.6% (expert and non-expert) of the study cases.

Tumor response evaluation with dynamic contrast enhanced (DCE / perfusion) MRI:

For the use of dynamic contrast enhanced (perfusion) MRI to assess response we found –
in a preliminary analysis – that the DCE parameter 'late slope' can predict if tumours will undergo a good or poor response to treatment with a sensitivity of 92%, specificity of 82%, positive predictive value of 80% and negative predictive value of 93%.

Lymph node staging with gadofosveset-enhanced MRI:

We found that particularly the sensitivity and negative predictive value to differentiate patients with lymph node metastases (N+) from patients without lymph node metastases (N0) improve after the addition of gadofosveset contrast-enhanced sequences to the standard (T2-weighted) MRI protocol. For the primary staging of nodes, sensitivity improved from 65% to 75% for non-expert radiologists and from 70% to 85% for expert radiologists; negative predictive values improved from 83-87% to 83-91%, respectively. For the restaging of nodes after chemoradiotherapy sensitivity improved from

63% to 82% for non-expert radiologists and from 70% to 83% for expert radiologists; negative predictive values improved from 80-90% to 83-91%, respectively. These results are in line with previously published pilot studies from our group.

For the primary staging of lymph nodes the addition of gadofosveset contrast-enhanced sequences led to an upstaging of the nodal stage in 7.7-15.3% of the cases for the expert radiologists and 8.8-11% for non-experts; conversely it led to downstaging of the nodal stage in 7.7-15.3% and 8.8-11%.. For the restaging of nodes after chemoradiotherapy the addition of gadofosveset contrast-enhanced sequences led to an upstaging of the nodal stage in 4.6-17.9% of the cases for the expert radiologists and 8.7-9.2% for non-experts; conversely it led to downstaging of the nodal stage in 6.2-7.1% and 4.6-13%, respectively

Interobserver agreement:

Interobserver agreement (IOA) - calculated using weighted quadratic kappa values with κ 0.00-0.20 indicating poor agreement, 0.21-0.40 fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 good agreement and 0.81-1.00 excellent agreement - to differentiate between patients with and without lymph node metastases was good (κ 0.70-0.75) both for standard T2-weighted and gadofosveset-enhanced MRI, for primary staging as well as for restaging after chemoradiotherapy. IOA to differentiate between patients with and without residual tumour after chemoradiotherapy was moderate, both on T2-weighted MRI as well as for diffusion-MRI.

List of Publications:

- Lambregts DMJ, Maas M, Bechers R, van Heeswijk M, Hupkens B, Houwers J, Peters N, Vliegen R, Kint P, Wijsman J, Mearadji B, Tanis P, Osinga-de Jong M, Belgers E, Ooms R, van Dielen F, Daniels-Gooszen A, Rutten H, Oudenhoven L, Faneyte I, Lahaye M, Beets G, Bakers F, Beets-Tan RGH. Diagnostic value of novel MRI techniques for the primary staging and restaging of rectal cancer: a multicentre study. Insights into imaging – ECR book of abstracts 2017;8(Suppl 1):S487
- Martens, M. H., Subhani, S., Heijnen, L. A., Lambregts, D. M., Buijsen, J., Maas, M., Riedl R, Jeukens CR,Beets-G:, KLuza E, Beets-Tan, R. G. Can perfusion MRI predict response to preoperative treatment in rectal cancer?. Radiotherapy and Oncology 2015; 114(2), 218-223.
- Lambregts D, Delli Pizzi A, Lahaye M, van Griethuysen J, Maas M, Beets GL, Bakers FCH, Beets-Tan R. A pattern-based approach combining tumor morphology with distinct diffusion-weighted MRI signal patterns for rectal tumor response evaluation after chemoradiotherapy. Dis Colon Rectum 2018;61(3):328-337
- Lambregts DMJ, van Heeswijk MM, Delli Pizzi A, van Elderen SGC, Andrade L, Peters NHGM, Kint PAM, Osinga-de Jong M, Bipat S, Ooms R, Lahaye MJ, Maas M, Beets GL, Bakers FCH, Beets-Tan RGH. Diffusion-weighted MRI to assess response to chemoradiotherapy in rectal cancer: main interpretation pitfalls and their use for teaching. Eur Radiol. 2017 Oct;27(10):4445-4454.
- M. Maas, G. Shakirin, D.M. Lambregts, M. Weibrecht, M. Perkuhn, M. Martens, R. Dijkhoff, G. Beets, R.G.H. Beets-Tan. Dynamic contrast enhanced MRI in rectal cancer: tumours with poor prognosis show low vascularity. ECR book of abstracts - Insights to imaging 2016; 7:162.