



ORIGINAL PAPER

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Infliximab MRI relaxation time in solution

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ABSTRACT

Introduction. The use of Quantitative Magnetic Resonance Imaging to drug monitoring *in vitro* or *in vivo* can provides a powerful means to map the effects of drugs on tissue activity.

Aim. The purpose of this study was to measure relaxation time of antibody phantom. For this purpose, infliximab sample was used.

Material and methods. The selected methods to detect relaxation time of antibody was Magnetic Resonance Imaging technique. We detected spin-lattice (T_1) relaxation time and discuss differences where compare to water.

Results. The measurements of spin-lattice (T_1) relaxation time showed significant differences. The results obtained in phantom indicate that we can use this result for measurements of relaxation time *in vitro*.

Conclusion. Infliximab is approved for severe cases of rheumatoid arthritis, together with methotrexate, for pronounced psoriasis and psoriasis-arthritis, ankylosing spondylitis as well as for chronic inflammatory bowel disease. We conclude, that Quantitative Magnetic Resonance Imaging can be used to monitor drug effects.

Keywords. infliximab, magnetic resonance imaging, relaxation time

Introduction

Quantitative Magnetic Resonance Imaging (QMRI) has already brought advances in diagnostic research.¹⁻⁵ Proton ¹H MRI has been already used to monitor a number of pharmaceutical processes e.g. to monitor the dosage form *in vivo* and correlate with *in vitro* behavior. The use of QMRI to drug monitoring *in vitro*

or *in vivo* can provides a powerful means to map the effects of drugs on tissue activity. Additionally, QMRI is important applications in pharmacological research. While standard MRI can provide basic information regarding tumour, the quantified QMRI can evaluate the effectiveness of drug therapy. Of particular interest are changes in drug relaxivity which are correlated

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Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 1.09.2018 | Accepted: 13.11.2018

Publication date: March 2019

with drug uptake.⁵⁻¹⁰ The aim of our study was to determine whether changes in spin-lattice relaxation time T_1 and spin-spin relaxation time T_2 allow monitoring the treatment with infliximab antibody. T_1 and T_2 in MRI are functions of spin density and also instrumental parameters such as the pulse sequence timing and slice selective sensitivity profile. At the same time valuable physiological information can be extracted from infliximab, while quantitative investigations of dynamics of drug delivery and drug effects is crucial for the development of effective therapy. Therefore, there is a growing interest in using MRI to examination of antibody drug such as infliximab.¹⁰⁻¹⁵

Material and methods

We have studied Infliximab using Magnetic Resonance Imaging techniques. Measurements of spin-lattice T_1 relaxation time were made using a 1.5 Tesla Magnetic Resonance Imager (Optima MR360 Advance, General Electric Healthcare). Three prepared phantoms:

- (1) infliximab solution
- (2) water
- (3) glue

were placed in the magnet. The samples were then scanned using Fast Spin Echo sequences with a coronal projection using a 4-channel small flex coil with a matrix size of 320×224 , a field of view of $10 \text{ cm} \times 10 \text{ cm}$, and a slice thickness of 2 mm. The T_1 relaxation time was measured using the saturation recovery method with a Time to Echo (TE) $TE=3 \text{ ms}$ and Time to Repetition (TR) $TR= 50 \text{ ms}, 100 \text{ ms}, 200 \text{ ms}, 300 \text{ ms}, 500 \text{ ms}, 700 \text{ ms}, 1000 \text{ ms}, 1500 \text{ ms}, 2000 \text{ ms}, 2500 \text{ ms}, 3000 \text{ ms}, 5000 \text{ ms}, 10\ 000 \text{ ms}$ and 15000 ms . Based on the generated image sequence, the MRI signal was collected from the region of interest that covered the same area in each sample.

Results

Here, we have investigated the QMRI response to infliximab. Infliximab is widely applied as a pharmacological drug. Pharmacological QMRI can tracks signal changes that reflect drug challenges and may be considered as a surrogate for changes in the gastroenterological processes. The QMRI images of 1) infliximab solution, (2) water and (3) glue showed the homogenous solutions of (1-3) phantoms. We observed that the relaxation time is increasing in direction (3) glue > (2) infliximab and (3) water. The changes in values due to proton density in phantoms caused changes in relaxivity values. The region of interest (ROI) in phantoms was selected in the same area in samples. The images became darker due to shorter T_1 values, that were associate with the loss of protons, decrease in water concentrations within the ROI. The measured values of relaxation time of (1), (2) and (3) phantoms are presented in Table 1.

Table 1. Relaxation time

T_1 -Water	T_1 -Infliximab	T_1 -Glue
3390 ms	2545 ms	2790 ms

Discussion

Infliximab is monoclonal antibody which contains a human constant region and a mouse-derived murine variable region. Infliximab is specific for human tumor necrosis factoralpha (TNF α). There is a rapid increase in the applications of MRI for molecular and cellular imaging in vivo an ex vivo. However, to study the cellular details of drug treatment, high resolution MR and long acquisition time are needed. MRI shows to be a useful technique for evaluation of infliximab. Studies in recent years have shown that MRI is essential for assessment of drug response. Therefore, in recent years, the use of MRI in patients with Crohn's disease has increased.¹⁻⁴⁶ MRI is sensitive to the anti-inflammatory effects of infliximab.¹ MRI of Crohn's disease patients identify predictors of deep remission on long-term maintenance anti-tumor necrosis factor α therapy.²⁻¹⁸ Magnetic resonance diffusion-weighted imaging was used after infliximab induction therapy in patients with Crohn's disease.¹⁹ Tumor necrosis factor antagonists can induce mucosal healing in patients with Crohn's disease.²⁰ Anti-tumor necrosis factor therapy heals many Crohn's disease.^{21,22} To evaluate the role of pelvic MRI in diagnosis and assessment of combined surgical and infliximab treatment of Crohn's disease.²³ MRI is used to assess the outcome of infliximab therapy in patients with perianal fistulizing Crohn's disease.²⁴⁻³⁴ Infliximab therapy, including loss of enhancing nodules and loss of meningeal enhancement.³⁵ MRI of infliximab, was used to evaluate the frequency and location of erosions.³⁶ MRI seems to be interesting for objective therapeutic evaluation and monitoring of patients with spondyloarthropathy.^{37,38} MRI examination was helpful in documenting the effect of treatment over this short period.³⁹ Patients who received infliximab therapy showed a decrease in spinal inflammation as detected by MRI.⁴⁰ In refractory rheumatoid arthritis patients, the addition of infliximab therapy may result in clinical, laboratory and magnetic resonance imaging improvement.⁴¹ MRI may have significant implications for the optimal use of expensive biologic therapies.⁴²⁻⁴⁴ MRI and clinical evaluation were performed before and after infliximab infusions.^{45,46}

Conclusion

Infliximab is approved for severe cases of rheumatoid arthritis, together with methotrexate, for pronounced psoriasis and psoriasis-arthritis, ankylosing spondylitis as well as for chronic inflammatory bowel disease. We conclude, that QMRI can be used to monitor drug effects.

Acknowledgment

Dorota Bartusik-Aebisher acknowledges support from the National Center of Science NCN (New drug delivery systems-MRI study, Grant OPUS-13 number 2017/25/B/ST4/02481).

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