A non-cardiac applications of T1-mapping

T1-maping w zastosowaniach niekardiologicznych

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KEYWORDS:

- T1-mapping
- non-cardiac applications
- MRI protocols

ABSTRACT

T1-mapping has proven to be a valuable tool in cardiac imaging. While mainly used in cardiac MRI, it is investigated for usage and application of T1-mapping to imaging of other organs and systems, including abdominal imaging, musculoskeletal imaging or neuroradiology, resulting in potential new prospects for medical imaging. T1-mapping provides numerical data on an inherent, physical property of imaged tissue – enabling quantitative and comparative assessment of tissue characterization f.ex. fibrosis, amyloid contents, fatty transformation, myelinization or contrast enhancement as well as lesion characterization.

Reports of application of T1-mapping in assessment of liver, kidney or pancreas fibrosis create perspectives of reducing the number of invasive diagnostic procedures, such as biopsies, as well as monitoring treatment response or disease progression. Furthermore T1-mapping can potentially replace MR elastography in assessment of liver fibrosis or used in thyroid fibrosis to define degree of destruction in AIT or other thyroid diseases. In neuroradiology T1-mapping is promising in the spine imaging, enabling better characterization of spinal cord lesions also has a potential to evaluate effectiveness of conservative or operative treatment. There are also successful reports of employing T1-mapping in orbital imaging, such as in predicting steroid resistant diplopia in Graves' disease or in evaluation of diabetic cataracts. In musculoskeletal imaging, T1-relaxation could be a possible biomarker of bone quality that could play a role in osteoporotic fracture risk assessment.

In conclusion, T1-mapping shows promise as a quantitative method complementary to standard MR imaging beyond cardiac MRI, and needs further research and validation efforts to establish its place in standard diagnostic protocols.

SŁOWA KLUCZOWE:

- T1-mapping
- pozakardiologiczne aplikacje
- protokoły MRI

STRESZCZENIE

Mapowanie T1-zależne okazało się cennym narzędziem w obrazowaniu serca. Jednakże prowadzone są badania pod kątem zastosowania mapowania T1 do obrazowania innych narządów i układów, w tym obrazowaniu jamy brzusznej, obrazowaniu układu mięśniowo-szkieletowego lub neuroradiologii, co daje potencjalne nowe perspektywy dla diagnostyki w medycynie. Mapowanie T1 dostarcza danych liczbowych na temat integralnych, fizycznych właściwości obrazowanej tkanki – umożliwiając ilościową i porównawczą ocenę jej charakterystyki, np. zwłóknienia, zawartości amyloidu, przemiany tłuszczowej, mielinizacji lub wzmocnienia kontrastowego, a także charakterystyki zmian ogniskowych.

Ponadto mapowanie T1 może potencjalnie zastąpić elastografię MRI w ocenie włóknienia wątroby, nerek czy trzustki lub być stosowane w diagnostyce i ocenie stopnia zwłóknienia i niszczenia tarczycy w AIT i innych chorobach tarczycy. Stwarza to perspektywy do ograniczenia liczby inwazyjnych procedur diagnostycznych, np. biopsji, a także do monitorowania odpowiedzi na leczenie czy progresji choroby. W neuroradiologii mapowanie T1 może być obiecujące w obrazowaniu kręgosłupa, umożliwiając lepszą ocenę uszkodzeń rdzenia kręgowego oraz ma potencjał do oceny skuteczności leczenia zachowawczego lub operacyjnego.

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Istnieją również udane doniesienia o zastosowaniu mapowania T1 w obrazowaniu oczodołów, na przykład w przewidywaniu podwójnego widzenia opornego na steroidy w chorobie Gravesa-Basedowa lub w ocenie zaćmy cukrzycowej. W obrazowaniu układu mięśniowo-szkieletowego relaksacja T1 może być możliwym biomarkerem jakości kości, który mógłby odgrywać rolę w ocenie ryzyka złamań osteoporotycznych.

Podsumowując, mapowanie T1 jest obiecującą metodą ilościową uzupełniającą standardowe obrazowanie MRI i wymaga dalszych badań i działań walidacyjnych w celu ustalenia jej miejsca w standardowych protokołach diagnostycznych.

Introduction

T1-mapping has proven to be a valuable tool in cardiac imaging, where it provides diagnostic clues on, among others, interstitial fibrosis, Fabry's disease or cardiac amyloidosis. This success in heart imaging has sparked an effort to apply T1-mapping to imaging of other organs and systems, including abdominal imaging, musculoskeletal imaging or neuroradiology, resulting in potential new prospects for quantitative medical imaging.

In most routine clinical MRI applications, only semi-quantitative data is achieved. MRI signal depends on T1-, T2* and T2- relaxation times, proton density (PD), or magnetic susceptibility of tissue. The MRI data obtained using various pulse sequences is reconstructed in such a way to achieve image contrast mainly dependent on, for example, T1- or T2- relaxation times. By this method T1-, or T2- weighed images are produced, where pixel brightness depends primarily, but not only, on T1- or T2 relaxation time. However, signal intensity measurements performed on routine T1- or T2 weighed images are not consistent between studies and are dependent on device calibration. T1-mapping on the other hand provides numerical data on an inherent, physical property of imaged tissue – its T1-relaxation time, thus enabling quantitative comparative analysis between subjects or in one subject at different time points. Quantitative assessment of tissue fibrosis, amyloid contents, fatty transformation, myelinization or contrast enhancement as well as lesion characterization are all potential applications of non-cardiac T1-mapping (1).

In this brief review, we present an overview on some T1-mapping's non-cardiac clinical applications presented in the literature.

Objective of the paper

Fibrosis in IgA-nephropathy

IgA-nephropathy is the most common cause of glomerulonephritis globally. An estimated 20-40% of those affected will progress to end-stage kidney failure over 20-years. Interstitial fibrosis is established to be one of the key factors contributing to kidney failure. Contrary to other common causes of glomerulonephritis, routine repeated kidney biopsies are not commonly performed because of a disadvantageous risk-to-benefit ratio. Thus, a non-invasive, reproducible, quantitative method is highly sought after, potentially serving as a mean to monitor treatment response. In their prospective, observational, single-center study Graham-Brown MP et al. (2) have compared T1-relaxation times of renal parenchyma in patients with IgAN and age-matched healthy subjects, showing significant and reproducible difference between those groups. One of the limitations of the study was small sample size (only 10).

Liver fibrosis

Liver fibrosis is a multifactorial global health problem gaining in significance, with prevalence rising in the past years. Complex pathophysiology and multiple etiologies create a need for robust severity assessment methods. Currently, MELD, ALBI scales (employing biochemical markers) as well as conventional or MR liver elastography are widely accepted in guiding patient management or assessing the prognosis in liver fibrosis. Hoffman et al. (3) studied a cohort of 223 patients with known or suspected liver fibrosis, aiming to assess

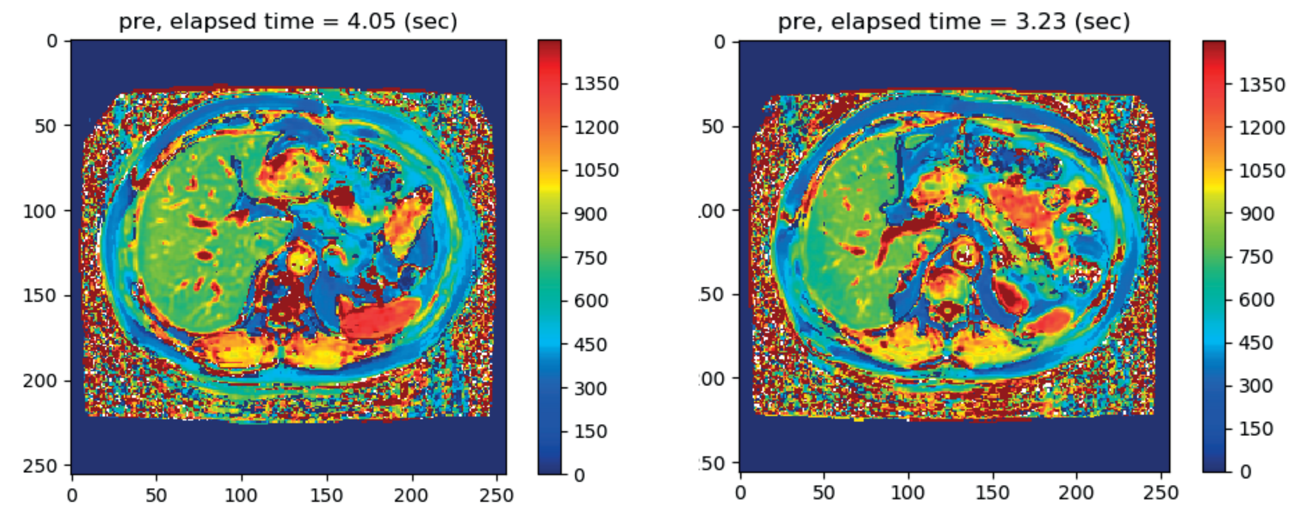

Figure 1 and 2. T1map of liver in MOLLI data calculation (4).

the correlation between liver parenchymal T1-relaxation time, liver stiffness assessed with MR elastography, and biochemical severity scales (MELD and ALBI).

T1-relaxation time was found to strongly correlate with liver stiffness as measured by MRE, as well as with MELD severity score. With an advantage of not needing additional hardware (as is the case in MRE) and still producing reproducible and clinically useful data, T1-mapping can potentially replace MR elastography in assessment of liver fibrosis.

Diabetic cataracts

Type 2 diabetes with its increasing prevalence and potentially debilitating sequelae is a global health problem. T2D increases the risk of developing cataracts, a potential cause of vision loss. Slit-lamp examination is the main diagnostic method of evaluating cataracts, but its use in assessing early-stage biochemical changes in lens composition is limited. In their prospective study of 56 subjects, Ma J et al. (5) explored the potential use of T1-mapping in evaluating lens status in patients with type two diabetes. They included 28 T2D patients (time from diagnosis >3 yrs.) with no lens opacity in slit-lamp examination and 28 age and sex-matched controls. T1-mapping showed statistically significant lens T1-relaxation time increase in the diabetic population, pointing to its possible usefulness in diagnosing and grading diabetic cataracts.

Autoimmune thyroiditis

Autoimmune thyroiditis (AIT) is the most common cause of autoimmune thyroid disease. Pathological mechanisms that contribute to the destruction of thyroid parenchyma include lymphocytic infiltration, fibrosis and apoptosis. In their case control study of 57 drug-naïve subjects, Liu J et al. (6) investigated potential links between T1-relaxation times of thyroid tissue and disease severity. They found a significant correlation between the increase of T1-relaxation time and degree of thyroid destruction (expressed as subclinical or overt hypothyroidism), as well as between T1-relaxation time and biochemical markers such as TSH, FT3, FT4, TPO antibodies or Tg antibodies. While ultrasound is the most common thyroid imaging method, it can only provide semi-quantitative data on AIT severity. T1-mapping can be potentially used to acquire quantitative data on thyroid fibrosis in AIT and other thyroid diseases.

Osteoporosis

Osteoporosis is a disease highly prevalent in post-menopausal women, where loss of bone mineral density and deterioration of internal bone structure leads to pathological fractures. Currently DEXA (Dual Energy X-ray absorptiometry) is the standard method of evaluating bone strength and fracture risk. However, DEXA provides information only on bone mineral density, while overall bone quality depends not only on the BMD, but also on geometric and structural defects of the cancellous bone. Therefore, a diagnostic method probing not only bone mineral density, but its overall quality, could become a fracture risk assessment tool superior or complementary to DEXA.

In their prospective study on four women scheduled for a hip arthroplasty procedure, Endo et al. (8) investigated the correlation between bone quality and T1-value. After performing pre-operative DEXA and MRI with T1-mapping, the patients underwent hip arthroplasty. The excised proximal ends of the femurs were preserved for following ex-vivo imaging (microCT and MRI) and biomechanical testing. A correlation between biomechanical bone quality markers (such as yield stress resistance) and T1-relaxation time was shown, and the authors concluded that T1-mapping could be a surrogate method for assessing fracture risk in osteoporosis.

Graves ophthalmopathy

Graves ophthalmopathy is an autoimmune inflammatory disease commonly synchronous with thyroiditis, where lymphocytic infiltrates and then fibrosis affect ocular muscles, impairing their function and leading to potentially debilitating symptoms such as diplopia. Orbital MRI (without T1-mapping) is a common diagnostic tool already established in management patients with GO, as it facilitates diagnosis and evaluates treatment response. CAS (Clinical activity score) is a standardized clinical index used conjointly with MRI to assess disease severity and treatment response. However, those diagnostic tools have shortcomings such as uncertain IV steroid treatment response prediction ability or lower robustness in the Asian population. Standard treatment for GO is IV glucocorticorticosteroid pulses, a therapy whose common and often severe adverse effects are widely known. IV steroid treatment is thought to counteract active inflammation (reduce lymphocytic infiltrates), while being ineffective against fibrosis. Therefore, accurately probing the degree of ocular muscle fibrosis could predict unsatisfactory response to steroid therapy. In their observational study, Matsuzawa et al. (8) explored a correlation between T1-relaxation time of ocular muscles and GO-associated refractory diplopia, concluding that T1-mapping could predict steroid response.

Cervical spinal cord compression

Degenerative cervical spinal cord changes are the most common cause of spinal cord lesions. Neurological symptoms often precede spinal cord signal abnormalities on conventional T1w and T2w imaging, so introducing a new imaging method more sensitive to spinal cord lesions could help select patients who could potentially benefit from surgery. Moreover, spinal cord compression is often intermittent and position-dependent. In their prospective, single center study on 41 patients, Maier et al. (9) confirmed the usefulness of T1-mapping in better characterization of spinal cord tissue appearing normal on conventional MRI. Though, further studies are needed to better characterize the link between T1-relaxation time and spinal cord injury degree, as well as to investigate T1-relaxation time changes in patients managed conservatively vs those managed operatively.

Conclusions

T1-mapping enables non-invasive, quantitative tissue characterization. While mainly used in cardiac MRI, it is investigated for use or already being used in numerous non-cardiac imaging applications. Reports of its use in liver, kidney and pancreatic imaging in assessment of tissue fibrosis create

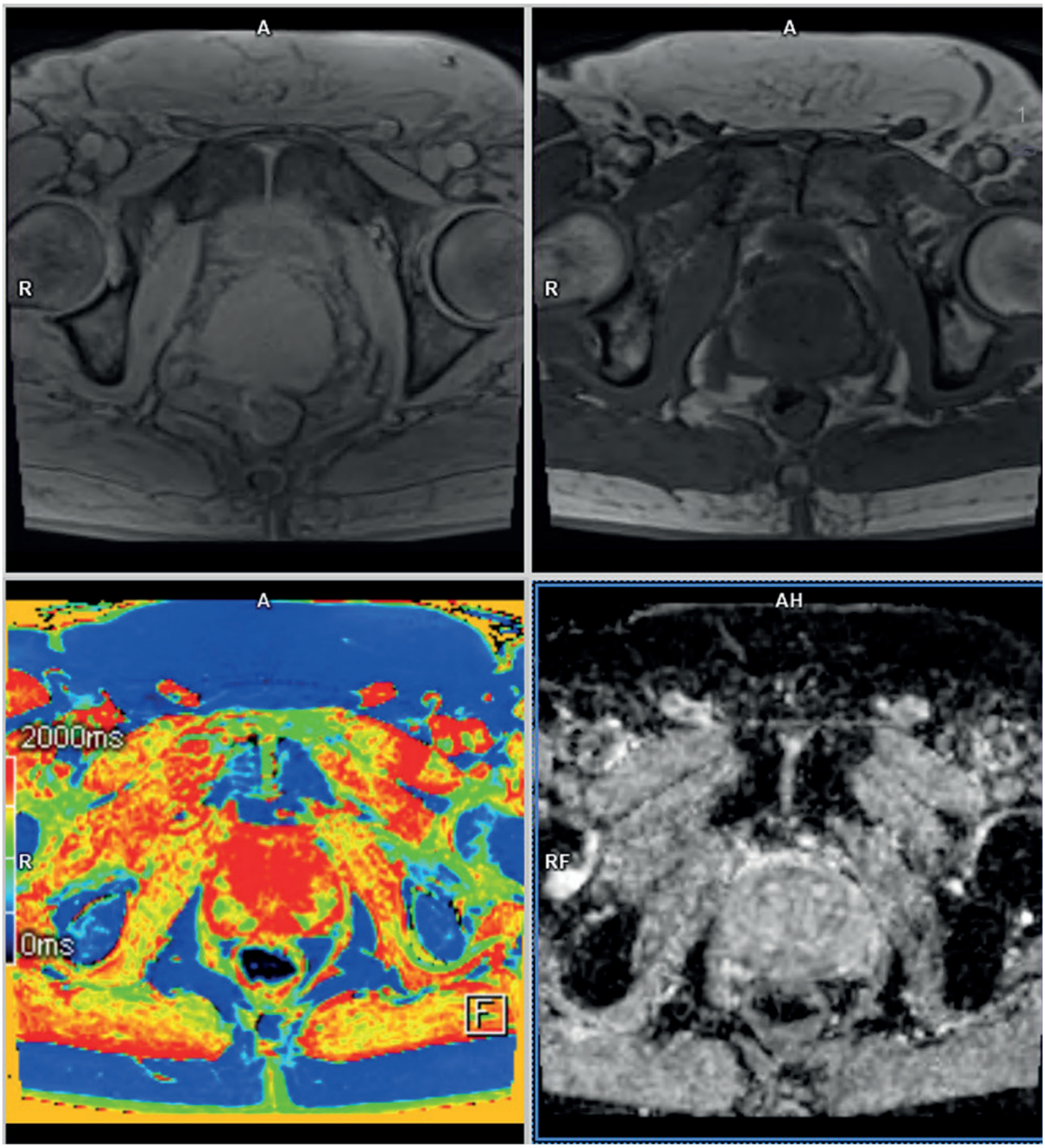

Figure 3. T1-mapping of the prostate gland in patient with PIRADS3 lesion in right PZpl and BPH.
Source: by courtesy of MD PhD Beata Ciszkowska-Łysoń, Mirai Clinic.

perspectives of reducing the number of invasive diagnostic procedures, such as biopsies, as well monitoring treatment response. In neuroradiology, T1-mapping is promising in the spine imaging, enabling better characterization of spinal cord lesions. There are also successful reports of employing T1-mapping in orbital imaging, such as in predicting steroid resistant diplopia in Graves' disease or in evaluation of diabetic cataracts. In musculoskeletal imaging, T1-relaxation could be a possible biomarker of bone quality that could play a role in osteoporotic fracture risk assessment.

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References

(1) Taylor AJ, Salerno M, Dharmakumar R, Jerosch-Herold M. T1 Mapping Basic Techniques and Clinical Applications. JACC: Cardiovascular Imaging 2016; 9(1):67-81. DOI:10.1016/j.jcmg.2015.11.005.

(2) Graham-Brown MP, Singh A, Wormleighton J, et al. Association between native T1 mapping of the kidney and renal

fibrosis in patients with IgA nephropathy. BMC Nephrology 2019; 20(1):1-7. DOI:10.1186/s12882-019-1447-2.

(3) Hoffman DH, Ayoola A, Nickel D, et al. MR elastography, T1 and T2 relaxometry of liver: role in noninvasive assessment of liver function and portal hypertension. Abdominal Radiology 2020; 45(9):2680-2687. DOI:10.1007/s00261-020-02432-7.

(4) Kim YC, Kim KR, Lee H, Choe YH. Fast calculation software for modified Look-Locker inversion recovery (MOLLI) T1 mapping. BMC Med Imaging 202; 21(1):26. DOI: 10.1186/s12880-021-00558-8.

(5) Ma J, Xu X, Wang S, Wang R, Yu N. Quantitative assessment of early Type 2 diabetic cataracts using T1,T2-mapping techniques. British Journal of Radiology 2019; 92(1103):1-5. DOI:10.1259/bjr.20181030.

(6) Liu J, Liu M, Chen Z, Jia Y, Wang G. Magnetic resonance T1-mapping evaluates the degree of thyroid destruction in patients with autoimmune thyroiditis. Endocrine Connections 2018; 7(12):1315-1321. DOI:10.1530/EC-18-0175.

(7) Endo K, Takahata M, Sugimori H, et al. Magnetic resonance imaging T1 and T2 mapping provide complementary information on the bone mineral density regarding cancellous bone strength in the femoral head of postmenopausal women with osteoarthritis. Clinical Biomechanics 2019; 65(2019):13-18. DOI:10.1016/j.clinbiomech.2019.03.010.

(8) Matsuzawa K, Izawa S, Kato A, et al. Low signal intensities of MRI T1 mapping predict refractory diplopia in Graves' ophthalmopathy. Clinical Endocrinology 2020; 92(6):536-544. DOI:10.1111/cen.14178.

(9) Maier IL, Hofer S, Eggert E, et al. T1 Mapping Quantifies Spinal Cord Compression in Patients With Various Degrees of Cervical Spinal Canal Stenosis. Frontiers in Neurology 2020; 11:1-8. DOI:10.3389/fneur.2020.574604.