

Health Sciences Doctoral (PhD) School

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**Development and optimisation of
an *in vivo* ^1H MR spectroscopic method
in healthy individuals**

PhD Thesis

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1. Introduction

The metabolite patterns in healthy and also in pathological brain can be determined with *in vivo* quantitative proton MR spectroscopic (^1H MRS) measurement. With clinical MR scanners molecules can be measured that consist hydrogen atoms with chemical bonds in forms of metin ($-\text{CH}$), methylene ($-\text{CH}_2$) and methyl ($-\text{CH}_3$) moieties. The proper level of quantification is very important in the application of *in vivo* MRS.

Quantitative measurements of metabolite concentrations would be of great importance as they would permit the comparability of data between different research sites and would also overcome the assumption that at least one metabolite concentration should be constant in the relative metabolite ratio approach. The main reason why absolute quantification of MR-visible metabolites is not widespread is the sometimes complicated technical or theoretical background necessary for the measurements.

Depending on the number of required corrections (T_1 , T_2 , B_1 etc.) during the MR spectroscopic measurement, data processing and calibration, comparison can be carried out in different levels of "absolute quantitative measurement". In case of good reproducibility a sequence- and scanner specific semi-quantitative results of the measurements can be specified in the so-called "institutional units". If the comparison between spectroscopic results and other methods is needed or we have to use the resulting concentration in the kinetic and thermodynamic equation, the use of standard biochemical units is required. Ideally it would lead to improvement to work out a measurement and evaluating method that does not need difficult correction steps making it possible for professional radiographers to do the measurements in everyday clinical practice.

Possible ways of the evaluation of MR spectroscopy

There are three main steps of quantitative spectroscopy: data collection (which includes localization), data processing (including model fitting) and calibration (change to standard units of concentration). In the latter the amount of metabolites signal must be defined in the spectrum, taken into account the number of protons of the given metabolite.

Depending on the number of necessary correlations (T_1 , T_2 , B_1 etc.) during the MR spectroscopic measurement, data processing and calibration, comparison can be carried out at different levels of “absolute quantitative measurement”. In case of good reproducibility such a sequence and scanner-specific semi-quantitative results of the measurement can be specify in the so called “institutional units”. If the comparison of spectroscopic results and other applied methods necessary or we have to use the resulting concentration in the kinetic and thermodynamic equation, the use of standard biochemical units required.

If we apply appropriate levels of correction during the measurement and postprocessing (B_1 , B_2 inhomogeneity, T_2 relaxation, partial volume effect, phase and base line correction etc.) than the area under the peaks will be precise enough and can be reproduced well. By comparing it with an external and internal reference we get the absolute concentration value.

During the measurements and spectra postprocessings steps theoretically it is possible to correct all sources of errors. In clinical practice in most of the cases it is not reasonable and there is no time for it. The more disturbing factors we can consider, the more precise the results of our measurements will be, at the same time we will be able to detect smaller and smaller changes of metabolic concentrations.

Different technical approaches of quantitative evaluation of MR spectroscopic measurement are known, that generally permit the quantitative determination of chemical substances with the application of a reference inside from the body (internal) or outside from the body (external). The advantage and disadvantages of both approaches are known. With the application of an internal reference the annoying parts of the necessary calibration and correction steps of external reference methods can be substituted with use of a proper internal reference, because of measurement conditions are the same for metabolites spectra and for reference substrates.

To avoid quantifications we have to determine the actual quantity of substrate applied as an internal reference. Water is a good candidate because of high amount of water in the brain. High signal-to-noise ration of water in MRS and MRI makes possible to separate liquor from intracellular water in the measured voxel, avoiding the effects of extracellular water compartments.

In vivo brain water content determination

For *in vivo* brain water content determination computer tomography was applied in the first experiments. Available physical parameters with MR imaging (for e.g. T_1 , T_2 , proton density) are also appropriate for brain water content determination.

FATOUROS and his colleagues developed a theory that explains the relationship between T_1 relaxation time and brain water content. FATOUROS and MARMAROU determined these formulas on the basis of fast exchange two-state model, that implies the interchange between free water molecules and bound hydration water fraction is sufficiently fast. T_1 relaxation time of the given tissue is the weighted average of T_1 relaxation times of free water and bound hydration water. We can assume that the total water content has a dominant role in relaxation processes and thus the tissue water content at any field strength can be estimated based on T_1 relaxation time (*Equations 1-3*).

$$1/f_w = ax + b/T_1 \quad \text{Equation 1}$$

$$1/f_w = 0,935 + 0,283/T_1; \text{ at 1T field strength} \quad \text{Equation 2}$$

$$1/f_w = 0,921 + 0,341/T_1; \text{ at 1.5T field strength} \quad \text{Equation 3}$$

Where f_w : percentage water concentration [%], that needed for the water map; T_1 : measured T_1 relaxation time [s]; 'a' and 'b': field strength and tissue hydration fraction dependent constants. (at 1T field strength $a=0.935$ and $b=0.283$; at 1.5T field strength $a=0.921$ and $b=0.341$).

2. Aims

According to the previously identified and described results in the literature our aims were the following:

1. To use brain water as an international reference for quantification of MR spectroscopic measurement.

1.a. At first it was necessary to validate the relationship between the T_1 relaxation time of water and brain water content at 1.5T—that was previously validated at 1T by others.

1.b. We would like to determine the water content of a given area of the brain with MR spectroscopy applying the validated relationship.

in an axial slice for the same distance and rotation relative to the AC-PC line, using a turbofast low-angle shot (FLASH) sequence with a slice thickness of 20mm.

The relaxation time T_1 was measured with an array of TRs (time of repetition) (940, 1300, 1700, 2400, and 4000 ms at 1T, and 1300, 1500, 3000, and 4000 ms at 1.5T). T_2 was likewise determined with an array of TEs (30, 100, 200, 400, 600, 800, 1000, 1200, and 1500 ms at 1T, and 20, 50, 80, 110, 140, 170, 200, 230, 270, and 300 ms at 1.5T). Other parameters of the applied stimulated echo acquisition mode (STEAM) sequence were identical: TR=6000 ms (T_2 measurement), TE=20ms (T_1 measurement), mixing time (TM) = 10 ms, preparation scans = 2, and acquisition = 1.

Water-suppressed scans (chemical shift-selective [CHESS] pulse, bandwidth = 35Hz) were collected only at 1.5T for metabolite concentration measurements with the following parameters: TR/TE/TM/acquisitions/voxel size = 6000ms/20ms/10ms/64/20×20×20mm³. The effects of both T_1 and T_2 on the spectra obtained with these parameters can be neglected, due to the short TE and TM, and sufficiently long TR. The total measurement time for a single voxel was 10 minutes 6 seconds.

Data processing

Spectroscopic raw data were post processed explicitly by using the Siemens Syngo-Spectroscopy software for spectroscopic analysis. We applied a Hanning filter and zero filling to 2048 data points before Fourier transformation. After baseline and phase correction, an automatic fit was applied to Fourier-transformed spectra, and the peak integrals of water, choline, creatine, and N-acetyl-aspartate were determined. The T_1 and T_2 values of water were obtained from the exponential fit (nonlinear least squares with Trust-Region algorithm) of the water peak integrals as a function of TR or TE, respectively.

The fraction of the slowly-relaxing component in the T_2 measurement was assigned to the CSF (f_{CSF}), and was used to correct for the partial volume effect in the quantification of the absolute metabolite concentration.

The MCW can be calculated (*Equation 4*) from the ratio of tissue water (f_w) and the molar concentration of water (55.6mol/l).

$$C = I_m \times MWC \times 2 / (n \times I_w) / (1 - f_{LIQU}) \quad \text{Equation 4}$$

Where C: molar concentration of the metabolite [mmol/l]; I_m : peak integral of a given metabolite; 2: it marks the number of the induced protons; MWC: molar tissue water

content was calculated from f_w and the molar concentration of pure water (MWC=55.6mol/l \times f_w); n: number of resonating protons; I_w : peak integral of water extrapolated to TE=0; f_{LIQU} : proportion of water in the liquor/100.

Measurements at 3 Tesla field strength

Materials

A total of six healthy volunteers (22 \pm 2 years) were involved in the study.

Methods – MR measurements

The examinations were performed at the Diagnostic Centre of Pécs on a 1T Siemens Harmony (Erlangen, Germany) and a 1.5T Siemens Magnetom Trio A Tim System (Erlangen, Germany) MR scanner. A standard circularly polarized head coil at 1T and a phased-array head coil at 3T were used also CP mode.

As a first step of calibration at 1T and 3T field strengths T_1 relaxation time measurements were performed in a given axial slice of the brain determined by anterior and posterior commissure (AC-PC) with identical position, resolution and slice thickness (FOV=220 \times 200mm²; matrix resolution 128 \times 128; slice thickness 15mm). According to the literature determination of AC-PC-line insures good reproducibility. For example on this basis, stereotactic neurosurgical interventions planned and carried out with millimeter accuracy.

We used a turbo flash sequence at 1T field strength with eight different time of inversion (TI), with the following parameters: (TR/TE=10,000ms/1.4ms; TI=200, 300, 500, 800, 1300, 1800, 3500, 6000ms. The time of acquiring an image was 30 seconds, and the measurement with the 8 TI took individually 4 minutes.

Fitting of T_1 times was performed for each voxels of the selected slice according to the **Equations 2** with Matlab R2007 programme. We converted the resulting T_1 values into a gray scale image to get a T_1 map. T_1 times at 3T were determined with a turbo spin echo sequences applying six different times of inversion; the previous calibration of the method was performed with phantom measurements. Parameters of the sequence: TR/TE=3000ms/11ms; TI=300, 600, 900, 1400, 2000, 2800ms. The measurement time was 45s; the full time was 4.5 minutes. We fitted the T_1 times with the help of the **Equation 3** voxel by voxel and then we got the T_1 map; where I: intensity; A and B: constants (include I_0); TI: time of inversion [ms]; T_1 : T_1 time [ms].

T₁ relaxation times and water content calibration

In the next step we correlated the calculated water content in every voxel acquired at 1T field strength to the T₁ values in homologue voxels at 3T. We found the following relationship between brain water content and T₁ relaxation time at 3T field strength (*Equation 5*).

$$f_w[\%] = (T_1 + 1217) / 31.85 \quad \text{Equation 5}$$

Applying this relationship at T₁ maps can be converted in to water map at 3T as well. The water map represents the water content in percentage. According to the relationship of that we set up, the brain water content can be determined at 3T field strength with T₁ measurement precisely.

Practical use of quantitative spectroscopy based on brain water content measurement at 3T

With the previously described MR spectroscopic method at 1.5T, the metabolite concentration of the brain can be determined. For this, we use the measured brain water content as an internal reference, that can be calculated using the correlation that we described (*Equation 5*). In the future it can be used at 3T field strength equipment.

Measurement of proton spectrum

Voxels were placed in the frontal white matter for the measurement of the white matter, and in the occipital gray matter for the measurement of gray matter. During the spectroscopic measurement we used water suppressed (CHESS) PRESS sequences at 3T field strength.

Spectra were measured with long repetition time (6000ms) and the shortest possible echo time (30ms) to reduce the effect of T₁ and T₂ weighting to minimum in the spectrum. The size of the measured voxel was 15×15×15mm³, the number of averaging were 96, the receiver bandwidth was 1200Hz/pixel.

Spectrum postprocessing was carried out Siemens Leonardo Workstation. After Fourier transformation, phase and baseline correction, the program fitted the metabolite curves, giving the necessary metabolite integrals for concentration calculation. The next step was the determination of the area belonging to one proton under the curve for the calculation of quantity of the metabolites. This can be derived from the water signals and measured water content.

Measurement of water signal

In each voxel we determined the integral of the water signal by the spectrum, that the concentration that belongs to this with T_1 measurement. We measured the water signal with the same parameters as the metabolite spectrums, the difference was that the water suppression was not switched on. T_1 measurement were performed with constant echo time and different repetition time: TR=6000, 5000, 4000, 3000, 2000, 1400, 900, 500ms; TE=30ms; bandwidth 2500Hz/pixel.

The size and position of the voxel was identical with the metabolite spectrum measurement. T_1 relaxation times were calculated with Matlab R2007 program, using water signal integrals measured with different repetition times. On the basis of T_1 relaxation times we determined the water content of the given white and gray matter areas.

T_2 measurement and concentration calculation

Separation of brain tissue water and liquor water content was based on T_2 relaxation time measurements. During T_2 measurements different echo times were: 30, 60, 90, 120, 180, 240, 400 and 800ms; TR was 3000ms. Other parameters were the same as in T_1 measurements.

We determined the T_2 relaxation times of the water content of the two compartments with Matlab R2007 using biexponential fitting. To the calculation of metabolite concentration we substituted the corrected integral of tissue water peak in to the relation introduced previously (*Equation 4*).

4. Results

Results at 1 and 1.5 Tesla field strength

With the increase of field strength T_1 relaxation time became longer. The calculated MWC proved to be slightly larger at 1.5T, despite the same voxel positioning.

No biexponential signal decay was observed in the white matter voxels during the calculation of T_1 relaxation time (i.e., no CSF fraction), whereas the gray matter voxels demonstrated the same f_{CSF} at the two field strengths, indicating good reproducibility ($10 \pm 3\%$ at 1T and $12 \pm 4\%$ at 1.5T, $P=.3$). The fit of functions applied to T_1 and T_2 calculations was nearly perfect with correlation coefficients of $R^2 < .99$ in each case.

In our study, the concentration of N-acetyl-aspartate in the gray matter ($14.02 \pm 1.93 \text{ mmol/l}$) was higher ($P < .05$) than that in the white matter ($11.08 \pm 2.24 \text{ mmol/l}$). We found a significantly higher ($P < .001$) concentration of creatine in the gray matter ($9.98 \pm 1.03 \text{ mmol/l}$) as compared with that in the white matter ($7.83 \pm 0.66 \text{ mmol/l}$). The difference in concentration of choline between the white matter ($2.05 \pm 0.38 \text{ mmol/l}$) and the gray matter ($1.14 \pm 0.24 \text{ mmol/l}$) voxels was also significant ($P < .001$).

Results at 3 Tesla field strength

The water content of each voxels in the water map made at 1T field strength were correlated with the T_1 values of homologue voxels measured at 3T field strength.

The strength of the linear correlation of water content and T_1 relaxation time is given by the correlation co-efficient (R^2), that is $R^2 = .8828$ at this time. This is a very strong correlation and it proves the solidity and precision of the fitting. The parameters of the fitted line: $a = 31.85 \pm 0.6\%$ and $b = -1217 \pm 1.0\%$; according to the $y = ax + b$ correlation (*Equation 6*).

$$f_w[\%] = (T_1 + 1217) / 31.85 \quad \text{Equation 6}$$

The measured T_1 relaxation times, compare to the results at 1T field strength, are longer. Water content values in the white matter are similar to that in the literature (67.6% vs. 68%), but our method resulted in a higher water content compare to literature data (83.5% vs. 80%).

Our gray matter results showed high variations may be because of partial volume effects. According to the applied voxel size ($15 \times 15 \times 15 \text{ mm}$) the measured volume inadvertently contains different volumes of white matter in every examination. The applied voxel position—the gray matter of parietooccipital region—is an accepted place for measurement of the gray matter.

The received molar tissue water content at 3T field strength of the gray matter is higher than at 1 and 1.5T, in the white matter it was lower than at 1 and 1.5T.

According to the biexponential T_2 relaxation time fitting contrary to the measured data at 1T and 1.5T biexponential fitting was successful in white matter, with high rate of deviation. In gray matter at 3T field strength the fraction of liquor water was smaller than at 1T and 1.5T field strength.

To correlate results to the measured data at 1.5T field strength it was smaller at 3T field strength. In our method there were no significant differences ($7.79 \pm 0.67 \text{ mmol/l}$ vs.

8.20±0.45mmol/l) between NAA concentration in the white matter and in the gray matter. Creatine concentration was significantly ($P<.05$) smaller in white matter (3.76±0.28mmol/l) than in gray matter (4.76±0.18mmol/l). Choline concentration was also significantly ($P<.05$) different (3.68±0.47mmol/l vs. 2.64±0.35mmol/l) in the measured voxels, but in this case it was significantly smaller in gray matter. Mio-inositol was present in significantly ($P<.05$) higher concentration in white matter (10.35±3.7mmol/l) than in gray matter (8.32±1.42 mmol/l).

5. Discussion

For the quantification of MR spectroscopic measurement there are many methods in the literature, the two main groups are the internal and external references. Water was applied as an internal reference previously, and an automatized protocol was developed based on the assumption of the water content of gray and white matter. Brain water content can change in different ages and in different pathological states. The relationship found by FATOUROS and his colleges makes possible the brain water content determination based on the T_1 value of water, that was validated at 1T field strength in different pathological states that increase the brain water content, for e.g. brain tumours and traumatic brain injuries. Our method yielded 40.53±0.57mol/l water content in white matter and 45.13±0.44mol/l in gray matter at 1.5T field strength based on T_1 value determination. According to data at 3T field strength gray matter water content is slightly higher (46.4±1.5mol/l), white matter water content is slightly lower (37.6±0.5mol/l). Our results shows good correlation with other MR and gravimetric methods from the literature.

Differences can be caused besides the different field strength, but can also one to the methods of T_1 relaxation time determination. At 1.5T field strength we used the equation worked out by FATOUROS and MARMARON, that resulted a slightly but significantly higher water content values in white matter and gray matter compared to the validated results at 1T. Beside this we validated the correlation of T_1 relaxation time and water content at 3T field strength with inversion time turbo flash sequences.

Use of the measured water contents and the water peak integral at TE=0 for calibration gave metabolite concentrations lying nicely in the range obtained by the meta-analysis of MRS results. For example, at 1.5T field strength determined metabolite concentrations in

white matter (NAA 11.28 ± 2.24 mmol/l) are the same with the values of outer reference determination methods. Metabolite concentrations from the gray matter is more difficult to correlate with the results of the white matter, and also data from the literature varies, because of regional differences and various partial volume effects (white matter, liquor). In white matter voxels the biexponential fit of T_2 relaxation curve was unsuccessful at 1T and 1.5T field strength. At 3T field strength fitting was successful—resulting in 2.65% small liquor fraction with high deviation (SD-value 2.51). Higher sensitivity at 3T field strength might explain detection of liquor water fraction.

Measurement of T_2 relaxation time permitted the extrapolation of water-signal to 0 echo time, so water peak integral at 0 echo time showed the whole water content (the repetition time was long enough compared to T_1 relaxation time). For metabolite determination we did not have to consider the effects of T_2 relaxation time because of short echo time of MR-sequence applied. This is an accepted method in the literature (long enough repetition time for full T_1 relaxation and short echo time to avoid T_2 relaxation effects).

There are two limiting factors of the applied method, that are related to MR-visibility of brain water content and water content determination based on T_1 relaxation time. The advantages of our method besides the two limiting factors, that there is no need for previous assumptions or difficult calibrations and special conditions that could prevent other methods of quantitative MRS from everyday use.

In conclusion, to the best of our knowledge, this is the first work to propose quantitative proton MRS based on the water content as an internal reference determined by T_1 measurement. We demonstrated, that the relationship between brain water content and T_1 relaxation time can be applied in human *in vivo* quantitative MR spectroscopy at 1.5T field strength. Metabolite concentrations, such as NAA, creatine, choline, mioinositol, calculated in this way show good accordance with values of other methods from the literature.

In MRS measurements higher field strength results in better signal-to-noise ratio also better peaks separation. The quality of the received spectrums is better, so the calculation of the peak integrals is more exact. During the application at 3T field strength the received metabolite concentration—in contempt of our exceptions—do not show good accordance with our previous results and also with data from the literature.

The explore the reasons further examinations are required in the future.

The proposed method is simple and can readily be applied in any MR center without the need for complicated corrections or calibration procedures.

Practical utilization of the results

The possible applications of the method developed by us in clinical practice and research may include the diagnosis and monitoring conditions and diseases involving changes in brain water content.

Our method that we applied on quantitative MR spectroscopy at 1.5T and 3T field strength can be used for examination of such conditions and diseases that do not affect T_1 relaxation time of brain tissue. In this way diffuse brain injury (for e.g. radiotherapy and toxic effects, the normal MR appearance of brain in multiple sclerosis, psychiatric disorders) could be the possible fields of application.

Scientific publications report of different application areas of quantitative MR spectroscopy with the application of other referencing methods:

- Characteristic metabolite level changes were found in the group of psychiatric diseases with mild cognitive impairment.
- In Duchenne muscular dystrophy decreased choline level were found in the cerebellum and in the temporoparietal region. The temporoparietal NAA concentration also showed mild but significant differences. The latter showed correlation with the patients' cognitive function.
- In childhood neurological processes, tumorous, inflammatory and infectious diseases, diseases affecting the white matter and in neonatal brain injury there are quantitative MRS applications. Differences of brain metabolite ratios proved to be important biomarkers and of prognostic value in prenatal hypoxia.
- The quantitative MRS could be of help in differentiation of low-grade and high-grade gliomas on metabolic basis.
- In multiple sclerosis conventional MR imaging shows brain lesions that show only partial correlation with the symptoms, progression and results of treatment. The quantitative MR techniques—including MRS—promote the understanding of the pathogenesis, the underlying processes of progression and the effects of treatment.
- With quantitative MR measurement methods (MR voxel-based morphometry, diffusion tensor imaging, functional MRI and MR spectroscopy) neurobiological and biochemical changes were detected in some psychiatric diseases. MR spectroscopy can

detect metabolic differences in specific brain areas in schizophrenia, bipolar disorder, mood disorders (uni- and bipolar), major depression, anxiety disorders and attention deficit hyperactivity disorder.

- In the corpus callosum decreased NAA concentration can be measured with quantitative MR spectroscopy and the differences detected in T_2 relaxation times relate to the pathology of schizophrenia and supports the previous hypothesis of decreased connections/"disconnectivity" in corpus callosum.
- To detect the effects of chemotherapy and radiation therapy on brain tissue a wide range of MR techniques were used; recently MR spectroscopy was also applied. Besides the differentiations of radiation necrosis from recurrent tumours, MR spectroscopy could play a role in the detection of changes in normal appearing brain tissue affected by the effects of radiation.

6. New scientific results

1. The previously validated correlation between T_1 relaxation time and brain water content at 1T was applied at 1.5T accomplished by a spectroscopic method. In gray and white matter of the brain we got the same results about the water content as in literature. Tissue water content was corrected with extracellular fraction based on biexponential T_2 relaxation time analysis.
2. It was successfully demonstrated that water content of the voxel can be determined reliably. We used water content calculated from MR spectroscopic T_1 relaxation time measurements at 1.5T, as an internal reference. We obtained metabolite concentrations in normal brain tissue equal with the previous data in the literature.
3. Water content measurement at 3T was calibrated using the previously validated brain water content determination based on T_1 relaxation time at 1T field strength. The coefficients of the equation about the relationship of T_1 relaxation time and water content were determined at 3T field strength.
4. We used the measured water content as an internal reference to quantify MR spectra at 3T.
5. The proposed method is simple and can readily be applied in any MR center and on any 1.5T and 3T MR scanners without the need for complicated corrections or calibration procedures.

7. Az értekezés alapjául szolgáló közlemények, absztraktok és előadások / Publications, abstracts and presentations

Az értekezés alapjául szolgáló közlemények / Publications

Az értekezés alapjául szolgáló közlemény idegen nyelven / Publication in foreign language

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Összefoglaló tudományometriai táblázat

MTMT adatbázis - Keresés - Bajzik Gábor tudományometriai adatai - Mozilla Firefox

mtmt.hu https://vm.mtmt.hu/search/osszefoglalo.php?sid=5V7qsJ35998553m60bVtJRw6Nvpn6P11&lang=0&vanlink=1&search=1&ponton=8&authorID=10020310

Tudományometriai adatok az MTMT adatbázis alapján
Készült az MTA követelményeinek figyelembe vételével
Bajzik Gábor táblázata megjelenítve: 2011. október 5. 19:19
Előző fokozat nincs megadva

Nyomtatás | Segítség | Levelek (0/0)

Tudományos közlemények áttekintő adatai (csak tudományos közlemények)

	közlemény (független / összes idézet)	magyar nyelvű	egyetlen szerzőként
Összes tudományos közlemény	180 (215/267)	123	16
Könyv szerzőként (monográfia, szakkönyv, lexikon vagy kézikönyv)	1 (3/4)	0	0
Könyvszerkesztés	1 (0/0)	0	0
Könyvrész, könyvfejezet (monográfia, szakkönyv, lexikon, kézikönyv vagy tanulmány)	3 (2/2)	2	0
Folyóiratcikk (lektoráltnak jelzett vagy IF-es teljes terjedelmű cikk)	38 (208/257)	20	1
Konferenciacikk (min. 4 oldal)	3 (0/0)	3	0
Absztrakt	69 (0/2)	43	2
Szabadalom	0 (0/0)	0	0
További tudományos közlemények	65 (2/2)	55	13
Összegzett impakt faktor (IF) /Teljes cikkek / hiányos cikkek / várható IF	44.265/41.299/0/2.966		
Összes idézet tudományos közleményekre	267		
Független idézet tudományos közleményekre	215		
Hirsch-index: "klasszikus", a függő idézeteket beleszámolva / csak független idézetekből számolva	6/6		

A programról Az adatbázis adminisztrátora: admin@mtmt.hu Lap teteje