


Szakmai záró beszámoló (Z)/ fenntartási jelentés (FJ)

(2012.01.01. után meghirdetett NKFI Alap pályázatok nyertes projektjei számára)

Projekt címe:	Implementation of BOLD MRI: a non-invasive, state-of-the-art method to assess renal hemodynamics and tissue oxygenation
Kedvezményezett(ek)(*):	(1) Dr. Hosszú Ádám (2) (3) (4) (5)
Projektvezető neve:	Dr. Hosszú Ádám
Projekt szerződött támogatási összege (Ft)	3 952 000.- Ft
Projekt szerződött saját forrásának összege (Ft)	0.- Ft
A projekt tényleges kezdési és záró időpontja (dátum):	2018.10.01. - 2019.01.31.
A projekt fenntartási időszakának hossza (X év); kezdési időpont (dátum):	4 hónap 2018.10.01.

(*) Konzorcium esetén kérjük minden Kedvezményezettet soroljon fel!


 Dr. Hosszú Ádám
 Projektvezető

1. Projekt célja

Renal ischemia/reperfusion injury (IRI)-induced acute kidney injury develops in various clinical conditions and is the main cause of graft loss following kidney transplantation (KTx). While KTx provides better long-term outcomes and reduced cost of treatment compared to dialysis, IRI is unavoidable and significantly influences graft function. Beside the shortage in donors, minimizing IRI and thus improving long-term graft function remains a major and yet unsolved problem.

At present, conventional markers of renal function such as serum creatinine and blood urea nitrogen are poorly-sensitive and poorly-selective. In addition, the imbalance between oxygen supply and demand in kidney tissue is the initiating step in the pathophysiology of IRI. Thus, non-invasive, *in vivo* imaging methods are indispensable for the adequate assessment of postischemic kidney function and oxygenation in both pre-clinical and clinical setups.

Blood oxygen level-dependent magnetic resonance imaging (BOLD MRI) is the most versatile, non-invasive imaging method available today. It has the advantages of superior spatial and temporal resolution which allow for the elucidation of pathophysiological changes in different anatomical regions of the kidney in the early stages of IRI. However, due to a lack of researchers proficient in the technique, it has not yet been introduced to nephrology research in Hungary.

The aim of the applicant was to become proficient in BOLD MRI experimental procedures and data collection. In addition, the applicant would like to gain experience at an institution founded by the ERC in order to successfully apply for an ERC Starting Grant in the near future.

2. A projektben vállalt eredmények bemutatása a projekt zárásakor, / a fenntartási időszak alatt

During the project Dr. Ádám Hosszú joined Prof. Thoralf Niendorf's laboratory at the Max Delbrück Center for Molecular Medicine, Berlin Ultrahigh Field Facility supported by an Advanced ERC Grant (ThermalMR, EU project 743077). Here he had the opportunity to learn from, and engage in discussion with several ERC grantees and scientists from the institution, which will help to improve his ERC Starting Grant submission.

In the first weeks of the project the awardee was introduced to the theoretical basics of magnetic resonance imaging, functional MRI techniques such as BOLD MRI, diffusion-weighted MRI and arterial spin labeled (ASL) MRI, as well as the optimization of imaging protocols. He familiarized himself with specific applications of BOLD MRI as well as rodent-specific experimental procedures. Using an imaging phantom (a specially designed object that provides consistent results without subjecting a living subject to direct risk) he learned the specific features of the 9.4 Tesla small animal scanner. He became proficient in geometry planning, MR image acquisition as well parametric mapping (T2 and T2*) of the kidney, followed by quantitative analysis.

In the second part of the project he performed *in vivo* mouse and rat kidney imaging. He was introduced to rodent-specific experimental protocols such as the monitoring of physiological parameters eg. breathing rate, heart rate, body temperature. Gating/triggering is very important during rodent MR scans, as breath-hold is not possible in rodents and motion artefacts can have detrimental effects on image quality.

A pilot study was performed on sham-operated, adult, male Wistar rats. Briefly, rats were anesthetized with 2 % isoflurane mixed with air of 500 ml/min and placed in the bore of the scanner on an animal bed. Local B₀ shimming that uses a voxel enclosing the kidney only was performed prior to T2/T2* mapping to improve B₀ uniformity. T2 mapping was conducted using a multi-spin echo sequence (repetition time=550 milliseconds; number of echoes=7; first echo time=10 milliseconds; ΔTE=10

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milliseconds; averages=1), T2* mapping was performed using a multi-gradient multi-echo technique (repetition time=50 milliseconds; number of echoes=10; first echo time=1.43 milliseconds; $\Delta TE=2.14$ milliseconds; averages=4). For analysis regions of interest were defined in the cortex, outer- and inner medulla and T2* values were determined.

These skills will allow for the non-invasive assessment of renal hemodynamics and tissue oxygenation, which will give essential information in the research of hypoxic kidney injury. Furthermore, the applicant will be able to implement this state-of-the-art method into ongoing pre-clinical research and in the future set up a core facility which provides access and expertise which would be beneficial for the entire nephrology community in Hungary.

Renal functional MRI techniques and results of the pilot experiment will be presented at the MATHINÉ Congress in May, 2019 in Budapest.

3. A tervezett, illetve ebből megvalósított célok, eredmények összevetése, differenciák indoklása

Due to the utmost difficulty of the model and time shortage, kidney isograft autotransplantation in rats could not be successfully performed. The pilot study was performed on sham-operated rats, while the transplantation experiment will be performed after the project leader's return to Budapest. As BOLD MRI image acquisition and data analysis are the same in sham-operated rats and ones that undergo kidney transplantation, this had no influence on the successful completion of the project and will not hinder the implementation of the technique into ongoing pre-clinical research in Hungary.

4. A projekt utóéletének bemutatása

Introducing state-of-the-art, non-invasive BOLD MRI imaging will be immensely profitable to our laboratory and to other researchers in Hungary. The opportunity to assess hemodynamics in the kidney and tissue oxygenation will give us essential information for drug development. The availability of such a non-invasive method will allow for better translation of our findings from experimental models to humans. Finally, a core facility providing expertise and access to such cutting-edge technology would be beneficial for the entire nephrology community in Hungary.

Based on his newly acquired experiences at an ERC-supported laboratory, the project leader will apply for an ERC Starting Grant to support his pre-clinical research in the future.

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5. A projekt indikátorai

5.1. Indikátor adatok

*Kérjük, hogy a szerződés mellékletét képező, pályázati adatlapon kitöltött **indikátormutatók teljesüléséről számoljon be tényszerű adatokkal!***

Indikátormutató megnevezése	Célérték	Tényleges érték	Teljesítést alátámasztó dokumentum
A fogadó intézmény ajánlólevele a projekt teljesítéséről	1	1	Ajánlólevél a fogadó intézmény vezetőjétől
Eredmények bemutatása hazai konferencián	1	1	A projekt befejezésének időpontjában még nem áll rendelkezésre

5.2. Egyéb a projekt indikátor adatainak teljesülésére vonatkozó megjegyzés

(max 1000 karakter)