ANALYSIS OF DNA DOUBLE-STRAND BREAKS IN HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS AFTER EXPOSURE TO 7T MRI

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Purpose and introduction. Magnetic Resonance Imaging (MRI) was primarily developed as a powerful diagnostic tool. This modality has experienced increasing demand over the past decades to also be used in the research with higher strength of the magnetic field (mainly 7T). Although ultra-high field magnetic resonance imaging (UHF MR) has been applied for 10 years with a very good safety record, the scientific basis for safe use in broader clinical applications is weak. Although most of the available literature reported no effects, a few studies have reported genetic damages after MRI. In particular, a recent study reported DNA damage detected after cardiac MRI and suggested similar restrictions as for ionizing techniques[1]. Further evidence for safe application of UHF MRI should address the question of potential genetic damage.

In this study, we assessed the impact of 7T MR scans on the induction of DNA double-strand breaks (DSBs) on human lymphocytes. DSBs are considered to be the most deleterious genetic lesions that can initiate carcinogenesis in human cells[2]. DNA damage has been the focus of research of several investigators since excess damage in somatic cells can lead to carcinogenesis while similar damage in germ cells can be transmitted to future generations[3].

Methods. Peripheral venous blood was drawn from 16 healthy volunteers (8 male; 8 female; age 25-58 years, mean 36 years). We separated the Peripheral blood mononuclear cells (PBMC) by density gradient centrifugation. To detect and validate the MR-related effects, particular care was taken in choosing ideal conditions for negative and positive control groups. Isolated PBMC suspension of each donor was divided into four sample tubes; unexposed, 7T static magnetic field (60 min), gradient echo-planar imaging (EPI) and X-ray-irradiation. The gradient echo-planar imaging (EPI) sequence was employed on a 7T whole-body MR scanner (Siemens AG, Healthcare Sector, Erlangen, Germany) and tailored to the maximum switched gradient as well as 100% specific absorption rate (SAR) in 1 hour scanning. We used immunofluorescence staining of phosphorylated serine 139 in the core histone variant H2AX (γH2AX) which forms a distinct focus at each break site in DNA strands[4]. Automated fluorescence microscopy (AKLIDES system) and flow cytometric analysis were used to quantify the γH2AX foci intensity immediately (0 hour) as well as 1 h and 20 h after the exposure in incubated cells at 37°C and 5% CO_2.

Results. As expected, the results showed a dose-dependent increase in DSB formation in all samples after exposure to ionizing radiation. In contrast, 7 T static magnetic field alone and combined with switched GR and RF pulses did not induce DSB formation in freshly isolated lymphocytes under the conditions applied (Fig1). Furthermore, no significant differences between 7T MR-exposed and unexposed cells could be observed analyzing the cell viability as well as proliferation behavior of subsequently phytohaemagglutinin (PHA) mitogen-stimulated PBMC.

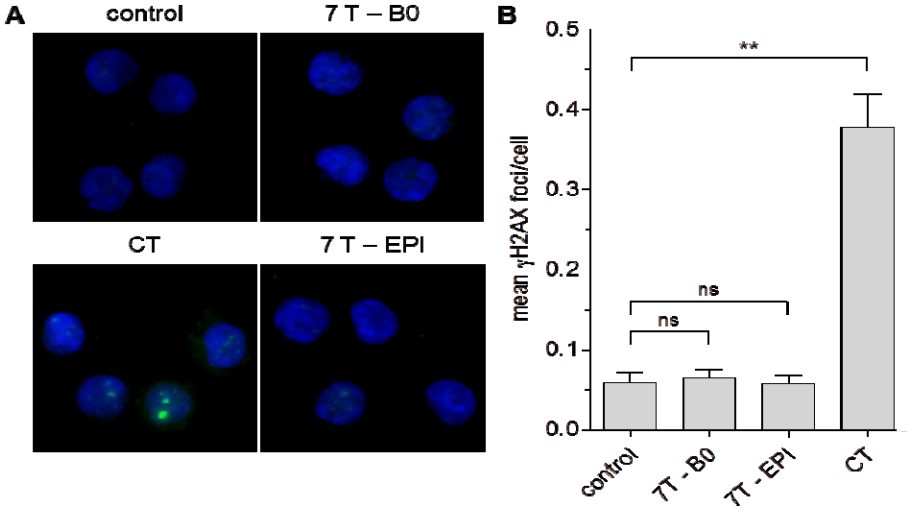

Fig 1. A. Visualization of the human PBMC and induced DSBs (green spots) with immunofluorescence staining method in four sample groups; Control (unexposed), Bo, CT and EPI. **B.** Mean number of γH2AX foci/cell in lymphocytes 1 h after exposure to indicated types of radiation. Diagram displays results of n = 16 independent experiments as mean ± SEM (**: $P < 0.01$; ns: $P > 0.05$)

Conclusions. In this study, we evaluated the impact of 7T MR-generated electromagnetic fields on the induction of DNA DSBs in human PBMC. We examined and compared the extent of damage with that observed in un-exposed and irradiated cells. Our results showed no significant increase in DSBs level, in all individuals, immediately (0 hour), 1 h and 20 h after UHF MRI exposure, compared to the unexposed group. Further, *in vitro, in vivo* and large scale epidemiological studies with sufficient statistical power which include several genotoxic endpoints, such as, chromosomal aberrations (CA) and micronuclei (MN) may further enrich the findings of the present study. Data from such comprehensive studies are useful to pave the way for ultra-high field (UHF) MRI to clinical adoption.

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