

## Case Report

---

# Safety of 9.4 Tesla for Neuroimaging of Healthy and For-Cause Volunteers

Keith R. Thulborn, MD, PhD<sup>1</sup>, Ian C. Atkinson, PhD<sup>1</sup>, Saad Jamil, BS<sup>1</sup>, Neil H. Pliskin, PhD<sup>2</sup>

<sup>1</sup>Center for Magnetic Resonance Research, University of Illinois at Chicago, USA

<sup>2</sup>Department of Psychiatry, University of Illinois at Chicago, USA

**\*Corresponding Author:** Dr. Keith R. Thulborn, Center for Magnetic Resonance Research, Room 1307, OCC, M/C 707, University of Illinois at Chicago, 1801 West Taylor Street, Chicago, Illinois 60612, USA, Tel: 847 830-0725; E-mail: [mrrix@ameritech.net](mailto:mrrix@ameritech.net)

**Received:** 01 May 2019; **Accepted:** 11 June 2019; **Published:** 17 June 2019

### Abstract

**Purpose:** To evaluate the safety of brain MR imaging examinations at 9.4 Tesla (T) as reflected in vital signs and cognitive performance in healthy and medically diagnosed adult volunteers as mandated by the regulatory agency of the Food and Drug Administration.

**Materials and Methods:** Vital signs were measured on healthy (N=22) and for-cause (N=24) adult volunteers positioned outside (0.3T) and at isocenter (9.4T) of a 9.4 T MR scanner before and after sodium (<sup>23</sup>Na) MR imaging. Cognitive performance was evaluated at the Earth's magnetic field before and after imaging. Measurements were compared for statistically significant changes due to exposure to the MR imaging at 9.4 Tesla static magnetic field.

**Results:** No statistically significant changes in the vital signs or cognitive performance were detected for either the healthy or subjects with medical diagnoses as a result of MR imaging at 9.4 Tesla.

**Conclusion:** Exposure to the static magnetic field and to MR neuroimaging at 9.4 Tesla do not have any readily demonstrated health risks reflected in alterations of vital signs or cognitive performance of healthy or for-cause adult volunteers.

**Keywords:** MRI safety; Ultra-high field MRI; Static magnetic field; Vital sign; Cognitive function

## 1. Introduction

Clinical magnetic resonance (MR) imaging has always been limited by sensitivity that is largely determined by the static field strength of the magnet. Human MR imaging in the 1970s operated at low magnetic fields of 0.1 and 0.3 Tesla because of the limited magnet technology and the perceived lack of penetration of RF energy into biological tissues [1,2]. This perception was radically changed as superconducting magnets allowed the introduction of 1.5 Tesla scanner for human imaging and spectroscopy in the early 1980s [3]. This field strength became the standard for state of the art clinical scanners for the next decade. Although MR image quality improved, signal-to-noise was still limiting. Despite considerable skepticism, a prototype 3 Tesla clinical scanner was introduced in 1993 [4], driven largely by the development of functional MRI using blood oxygenation level dependent (BOLD) contrast [5-8]. The magnetic susceptibility changes of blood that form the basis of BOLD contrast increases almost quadratically with magnetic field strength [4,9]. Not only was human fMRI dramatically improved, but clinical trials also showed greatly improved human brain anatomy that resulted in the first FDA cleared 3T scanner being introduced in 1999 [10]. Magnet manufacturing technology continued to evolve, leading to the first and only 8 Tesla scanner for human MR imaging [11]. The conservative research community pushed for 7 Tesla scanners which have received wide acceptance around the world [12]. The first 7 Tesla scanner approved by the FDA for clinical use was recently delivered [14]. Meanwhile, magnet manufacturing technology has evolved allowing higher field human sized magnets to be produced at 9.4 Tesla [15,16] and 10.5 Tesla [17].

Since 1982, the United States Food and Drug Administration (FDA) has maintained guidelines for human exposure to static magnetic fields [18]. After originally being set at 2T, the guideline was revised to 4T in 1997, and revised again to its current value of 8T in 2003. No subsequent revisions have been made despite higher field magnets and potential new and improved human clinical applications. Initial results [19-25] from ultra-high field systems have demonstrated emerging human applications, but safety remains an important topic for human applications at ultra-high field. Much early speculation and theoretical analysis [26, 27] about the safety of ultra-high field imaging and some early occasional dire predictions [28, 29], have appeared in the scientific literature. However, such sensational predictions as bulk water splitting have been shown to be unlikely to ever occur in human imaging [26]. Despite skepticism about the safety risks of long term adverse biological interactions of ultrahigh magnetic fields, the FDA and institutional review boards demand data to support this contention.

Two reports have already demonstrated the safety of human MR imaging at 9.4T in normal adults [30, 31] performed within the FDA guidelines for gradient switching and specific absorption rate (SAR). Additional investigations have been reported on the safety of MR imaging up to 8T [32-34] and of human exposure to the fringe fields of ultra-high field systems [35]. These reports have focused on healthy volunteers and reported the well-known transient sensory effects, such as vertigo or a metallic taste, but none found a safety risk. The consensus of the published ultra-high field MR safety studies is that exposure to ultra-high field MR imaging does not pose an immediate demonstrable health risk for normal adult volunteers.

This work presents the safety data on exposure of for-cause volunteers (volunteers with a medical diagnosis) to ultra-high field MR imaging and presents additional data for healthy volunteers. Although no differences are expected between normal and for-cause subjects, the experimental data for normal subjects was requested before approval for scanning of for-cause subjects was provided by the FDA and by the IRB. These experimental data can be used by other researchers to decrease the concerns of the regulatory agencies that demand experimental safety data. The acquisition of such data places a large burden on limited research resources.

## **2. Materials and Methods**

### **2.1 Human subjects**

Since this 9.4T device operates above the 8T insignificant risk guideline, an investigational device exemption (IDE) was granted by the FDA for this Institutional Review Board (IRB) approved research. Written informed consent was obtained from 22 healthy volunteers (13 male) aged 22-77 years (average 49.5 years) and 24 for-cause volunteers (8 male) aged 26-78 years (average 42.9 years). The for-cause group was made up of patients with specific clinical diagnoses including brain tumor (N=7), migraine (N=2), seizure (N=1), electrical trauma (N=4), traumatic brain injury (N=3), papilledema (N=1), dementia (N=1), aphasia (N=1), weakness (N=2), cerebrovascular disease (N=1), and depression (N=1). Individuals with a non-MR compatible implanted medical device, claustrophobia, or other contraindication to MR imaging were excluded from the study. Female subjects of childbearing potential were screened for pregnancy verbally, but also with a urine test as demanded by the Institutional Review Board. No subjects were excluded verbally or by pregnancy testing.

A short entrance interview immediately prior to imaging was given to assess the subject's anxiety and comfort. Subjects were screened for metal objects using a metal detecting wand (Garrett Metal Detectors, Garland, TX) to minimize the risk of objects becoming projectiles in the magnetic field of the 9.4 T MR scanner.

### **2.2 Cognitive assessment**

Cognitive testing data were collected before and after 9.4T MR imaging. Cognitive testing consisted of the Hopkins Verbal Learning Test - Revised (HVLT-R) [36], the written (SDM-W) and oral (SDM-O) versions of the Symbol Digit Modalities (SDM) [37], the 200 items Paced Auditory Serial Addition Test (PASAT-200), and the Letter Number Sequencing (LNS) subtest from the third edition of the Wechsler Adult Intelligence Scale [38]. These tests have been used to assess cognitive function in previous MR safety studies [30,31] and are used routinely in clinical evaluations. All cognitive testing was performed in the earth's magnetic field in a private, quiet testing room. Alternate versions of the HVLT-R and the SDM were used to avoid practice effects. The PASAT-200 was only administered once per subject (either before or after imaging) to avoid the large practice effect that is known for this test [39]. All other tests were given both before and after imaging. Test forms and PASAT-200 administration time (pre vs. post imaging) were randomized among subjects. Participants were not given performance feedback during the testing. Each cognitive testing session lasted between 15 and 25 minutes.

### 2.3 Vital signs assessment

Vital signs were monitored before, during and after 9.4T MR imaging. These non-invasive measurements were made using an MR-compatible patient monitoring system (Precognis, InVivo Corp, Jacksonville FL). Heart rate, respiratory rate, blood pressure, end-tidal carbon dioxide (ETCO<sub>2</sub>), and peripheral arterial oxygen saturation percentage (O<sub>2</sub>-sat) were measured three times at approximately one minute intervals with the subject lying supine with a leg support under their knees, with their head in the radiofrequency (RF) coil, and blankets covering them for warmth. The triplicate measurements were taken with the subject's head positioned outside the magnet at 2.6 m from isocenter in a magnetic field of approximately 0.3T and again while at isocenter in a magnetic field of 9.4T. Subjects were moved into and out of the magnet bore at a constant rate of less than 4 cm/sec. This maximum rate has been found to minimize the discomfort of moving through the fringe field gradient to isocenter of the static magnetic field of the 9.4T magnet. The vital sign measurements were repeated after imaging while the subject's head was at 9.4T and again after being removed from the magnet back to 0.3T.

### 2.4 Subjective assessment of the MRI experience

Subjects completed a short verbal exit interview to assess their experience of participating in this research protocol. The interview included questions about discomforts commonly experienced during exposure to strong static magnet fields (e.g., vertigo or metallic taste) as well as questions about participant anxiety and comfort. Participants were encouraged to give complete details (e.g., intensity, frequency, and duration, time and location sensation experienced) about any sensations experienced.

## 3. Data Analysis

### 3.1 Cognitive assessment

For-cause and healthy subjects were analyzed separately for all cognitive test analyses. The cognitive performance tests were scored and the raw performance data were analyzed for each test. The PASAT-200 performance data were analyzed with a one-way ANOVA to test for a statistically significant change in performance due to 9.4T MR imaging (before vs. after imaging) at a 95% confidence level. Data from each remaining cognitive test were analyzed with a one-way ANOVA with repeated measures for a statistically significant change in performance due to 9.4T MR imaging (before vs. after imaging) at a 95% confidence level. A small number of subjects did not complete some of the post-imaging, cognitive testing due to fatigue or by time constraints imposed by the subjects. Test data from these subjects were removed from the analysis.

### 3.2 Vital signs assessment

The for-cause and healthy subjects were analyzed separately. The vital sign data were analyzed for statistically significant changes due to exposure to either the 9.4T static magnetic field or non-proton MR imaging. A two-way analysis of variance (ANOVA) with repeated measures was performed on the measured data for each vital sign type to test for changes attributable to magnet field strength (0.3T vs. 9.4T) and 9.4T MR imaging (before vs. after imaging) at a 95% confidence level. There were not enough for-cause subjects to analyze each disease type

separately. Data were censored from analysis when recognizable technical problems prevented accurate data collection. The most common cause for censoring was the nasal cannula not remaining in position, leading to unreliable ETCO<sub>2</sub> and respiratory data. Since the subjects were provided noise isolating earphones, the nasal cannula had to be taped in place rather than being secured around the ears as is normally done. This leaves the cannula more susceptible to being dislodged when the subject is moved into and out of the magnet.

### 3.3 Imaging protocol

All data were collected using a custom-built 9.4T MR scanner (80 cm diameter warm bore) optimized for human brain imaging [15]. Non-proton MR imaging was performed using a custom-built sodium (<sup>23</sup>Na) birdcage RF coil tuned to 105.92 MHz. A maximum of 60 minutes of sodium imaging was permitted by the Institutional Review Board on each subject. Imaging had to remain within the current FDA guidelines for gradient switching and SAR. Only the 9.4T static magnetic field was outside the FDA insignificant risk guidelines. The maximum gradient amplitude and slew rate used for imaging were 5.47 mT/m and 150 mT/m/ms, respectively. The global SAR was monitored in real-time and the total value (watt-seconds) accumulated for all acquisitions was recorded. Individual acquisitions were completed in less than 10 minutes using a flexible twisted projection imaging (flexTPI) acquisition [40]. Subjects wore earplugs and noise isolating headphones during imaging.

## 4. Results

All 46 subjects completed the protocol without incident. One for-cause subject withdrew prior to imaging due to discomfort from the “spinning feeling” experienced while being moved into the magnet. On average, subjects underwent  $46.7 \pm 10.2$  minutes of imaging and accumulated  $13,223 \pm 4,420$  watt-seconds of energy exposure. Tables 1 and 2 summarize the p-values from the analyses of cognitive test performance and vital sign data, respectively. Table 3 shows the number and details of subjects reporting various sensations. The most commonly reported sensation was sleepiness (healthy=9, for-cause=8) and nervousness (healthy=4, for-cause=6).

## 5. Discussion

After accounting for multiple comparisons, none of the cognitive performance or vital sign data were statistically significant at a 95% confidence level. This matches the findings of previous safety investigations [30, 31], but extends this finding to for-cause subjects for the first time at 9.4T. Although not unexpected, regulatory agencies have demanded experimental data in both normal and for-cause subjects in the evaluation of safety at this higher field. Individually, only one cognitive test and four different vital sign measurements were found to be significant (p-value < 0.05).

Only the oral version of the Symbol Digit Modalities cognitive test (SDM-O) given before and after imaging was found to have a significant change (p< 0.05) and only for the for-cause subjects (Table 1). The written version showed no significant changes. Although significant, the change is not regarded as clinically significant with only a marginal decrease in average performance from before (SDM-O score= $53.5 \pm 12.0$ ) to after (SDM-O score= $49.4 \pm$

11.9) imaging. No change in performance on SDM-O was found for the healthy subjects. The other cognitive tests showed no significant changes in performance from exposure to 9.4T imaging in normals or for-cause subjects.

The vital sign data (Table 2) and the review of the original vital sign data over time (not shown) revealed no clinically significant safety concerns and any statistically significant changes were not clinically significant. The O<sub>2</sub> saturation of healthy subjects decreased less than 1% between outside the magnet (0.3T) and at magnet isocenter (9.4T) locations. This small change was not observed in the for-cause subjects or in previous studies and is within the error of this measurement for the equipment used. The average O<sub>2</sub> saturation throughout the study remained above 95%.

	N		9.4T Imaging (p-value)	
	Healthy	For Cause	Healthy	For Cause
<b>HVLT</b>	22	22	0.553	>0.999
<b>SDM-O</b>	21	22	0.511	<b>0.032</b>
<b>SDM-W</b>	22	22	0.692	0.584
<b>LNS</b>	22	19	0.108	0.805
<b>PASAT-200<sup>A</sup></b>	22	19	0.820	0.196

**Table 1:** Statistical analysis of cognitive performance data. Data are analyzed as paired data (before and after 9.4 Tesla imaging) for each subject. No differences within groups or between groups were found. The difference in numbers (N) across tests is because a small number of subjects did not complete all cognitive tests.

Comparisons	N		Before and After 9.4T Imaging (p-value)		0.3T and 9.4T Magnetic Field Strength (p-value)		Interaction (p-value)	
	Healthy	For Cause	Healthy	For Cause	Healthy	For Cause	Healthy	For Cause
<b>Pulse</b>	20	22	0.090	0.121	0.681	0.455	0.147	0.492
<b>Systolic BP</b>	22	23	0.139	<b>0.013</b>	0.344	<b>0.031</b>	0.301	0.140
<b>Diastolic BP</b>	22	23	0.223	0.176	0.338	0.067	0.163	0.233
<b>Respirations</b>	21	20	0.450	0.418	0.970	0.988	0.918	<b>0.021</b>
<b>O<sub>2</sub> Saturation</b>	20	22	0.109	0.876	<b>0.016</b>	0.170	0.383	0.859
<b>End-Tidal CO<sub>2</sub></b>	21	19	0.739	<b>0.035</b>	0.408	<b>0.001</b>	0.414	0.646

**Table 2:** Statistical analysis of vital sign data. Data are analyzed as paired data for each subject. No differences within groups or between groups were found. The difference in numbers (N) across the vital signs was because technical limitations prevented accurate data collection in a small number of cases.

The systolic blood pressure of for-cause subjects was lower after imaging ( $119.6 \pm 17.3$  mmHg) compared to before imaging ( $121.9 \pm 18.0$  mmHg). Similarly, it was also lower on average when the subjects were at magnet isocenter ( $119.21 \pm 16.87$  mmHg) than when they were 2.6 m from isocenter in a field of 0.3T ( $122.28 \pm 18.31$  mmHg). Both of these changes are likely due to the subjects lying supine and becoming more relaxed as the study progressed; several subjects reported sleeping during imaging. Inspection of the systolic blood pressure over time for the for-cause subjects revealed that the highest average blood pressure was measured at the beginning of the study, before entering the magnet with the subject's head in a field of 0.3T. This measurement is most susceptible to bias from anxiety of participating in the study, an effect that has been previously observed [30].

Condition	Healthy	For-Cause
Vertigo/spinning/lightheaded	13 <sup>a</sup>	5 <sup>A</sup>
Temperature	5 <sup>b</sup>	5 <sup>B</sup>
Nervousness	4 <sup>c</sup>	6 <sup>C</sup>
Sleepiness	9	8
Metallic Taste	1 <sup>d</sup>	1 <sup>D</sup>
Muscle twitching/tingling	6 <sup>e</sup>	4 <sup>E</sup>
Unusual smells	1 <sup>f</sup>	1 <sup>F</sup>
Flashing lights	1 <sup>g</sup>	0
Other	1 <sup>h</sup>	1 <sup>H</sup>

**Table 3:** Reported sensations reported during entrance and exit interviews.

<sup>a</sup>One subject reported feeling lightheaded when sitting up after imaging. Other subjects reported vertigo or a “spinning sensation” when being moved into or out of the 9.4T scanner; <sup>A</sup> Subjects reported vertigo or a “spinning sensation” when being moved into or out of the 9.4T scanner; <sup>b</sup>Subjects reported being cold during imaging or while in the scanner; <sup>B</sup>Three subjects reported being cold during scanning. One subject reported feeling a slight increase in temperature during one acquisition but not all acquisitions. One subject reported feeling cold during most acquisition and slightly warmer during one acquisition; <sup>c</sup>Three subjects reported feeling nervous about the imaging or during the imaging. One subject reported anxiety due to the proximity of the RF coil; <sup>C</sup>Five subjects reported feeling nervous about the imaging. One subject reported nervousness due to “feeling cramped” during the study; <sup>d</sup>Subject reported experiencing a metallic taste when being moved into the scanner; <sup>D</sup>Subject reported that they always have a metallic taste but experienced a slight increase in the sensation when being moved into the scanner; <sup>e</sup>One subject reported having “restless leg syndrome” and also feeling a tingling in the mouth near a dental implant. One subject reported tingling and twitching in the toes throughout scanning. One subject reported tingling in the hand before any imaging. Three subjects reported non-continuous twitching/tingling during no more than two acquisitions; <sup>F</sup>Three of the subjects reported muscle twitching or tingling during the entrance interview and that they



always feel this sensation. One subject reported a “tingling” sensation when entering the scanner but not during imaging; <sup>F</sup>Subject reported smelling “roses” before the first data acquisition; <sup>F</sup>Subject reported smelling “ether” when inside the RF coil, which may have been the scent of the solution used clean the coil between subjects; <sup>E</sup>Subject reported seeing “lights” when being moved into the scanner and having dry eyes while in the scanner; <sup>H</sup>Subject reported that their right elbow “fell asleep” during imaging; <sup>H</sup>Subject reported having a headache before imaging.

Despite the small p-value for the interaction effect for the respiratory rate measured in the for-cause subjects, the respiratory rates varied by less than a 0.5 respirations per minute for the average respiration rates measured from before to after imaging and from 0.3T to 9.4T exposure. This is not clinically significant. Likewise, the end-tidal CO<sub>2</sub> measured in the for-cause subjects decreased from 37.0 ± 6.0 mm Hg to 35.6 ± 5.7 mm Hg from before to after imaging. This small change was not clinically remarkable or observed in the healthy cohort.

The experiences (Table 3) reported by the subjects were consistent with previous investigations [30, 31] and not considered health risks. All subjects described the sensations as mild. Only one for-cause subject requested to be removed from the magnetic field after experiencing a “spinning feeling”. Subjects commonly reported experiencing vertigo, spinning, or lightheadedness (healthy=13, for-cause=5). This was reported almost exclusively when being moved into or out of but not while stationary in the magnet. This is a well-known sensory effect that has been reported in several ultra-high investigations [30, 31] and is considered harmless. In all cases, the vertigo stopped once the subject was stationary. A small number of subjects reported a temperature change (healthy=5, for-cause=5). The majority of these subjects indicated feeling cold during imaging (healthy=5, for-cause=4), consistent with previous data [30, 31]. The temperature of the 9.4T magnetic room is controlled at 65°F. Two for-cause subjects reported feeling warmer during a single acquisition, one of whom also felt cold during other acquisitions. Muscle twitching or tingling was reported (healthy=6, for-cause=4), although few stated it occurred during imaging and none reported pain. All imaging was performed at lower slew rates ( $\leq 150$  mT/m/ms) and amplitudes ( $\leq 5.47$  mT/m) than are routinely used for clinical MR imaging. The frequency of visual, gustatory and olfactory sensations was low and consistent with previous investigations.

Removing the reports of sleepiness, nervousness, coldness, and sensations reported during the entrance interview, approximately half of all subjects report no sensation of any kind (healthy=6, for-cause=16). This suggests that exposure to the 9.4T static magnetic field and the MR imaging was tolerated by the healthy and for-cause subjects and extends the findings from 8 Tesla [32-34, 41].

The absence of any statistically significant and clinically remarkable changes to cognitive performance or vital signs is consistent with previous investigations of human exposure to ultra-high static magnetic fields. The data for healthy subjects supports the existing data on healthy volunteers. This is the first report of similar results for for-cause subjects at the ultra-high static magnetic field of 9.4T. The lack of any readily demonstrable irreversible effects suggests that 9.4T MR imaging performed within the current FDA guidelines for SAR and gradient



switching can be performed safely in both healthy and for-cause subjects. These data are not surprising and should provide experimental data for other ultrahigh field researchers to satisfy concerns of regulatory agencies without being burdened with the prolonged safety testing beyond that done for routine clinical imaging.

Although the biological impact of static magnetic fields is not a safety issue, the “missile effect” of magnetic materials including medically implanted devices inadvertently introduced into the magnetic field should not be ignored. Screening should be strictly enforced when safety data for a device are not available.

### **Acknowledgement**

The authors gratefully acknowledge financial support from the PHS RO1 CA CA1295531. Financial assistance was provided by the University of Illinois at Chicago and the Chicago Biomedical Consortium SPARK award.

### **References**

1. Hoult DI, Lauterbur PC. The sensitivity of the zeugmatographic experiment involving human samples. *J Magn Reson* 34 (1979): 425-433.
2. Bottomley PA, Andrew ER. RF magnetic field penetration, phase shift and power dissipation in biological tissue: implications for NMR imaging. *Phys Med Biol* 23 (1978): 630-643.
3. Bottomley PA, Hart HR, Edelstein WA, et al. Anatomy and metabolism of the normal human brain studied by magnetic resonance at 1.5 Tesla. *Radiology* 150 (1984): 441-446.
4. Thulborn KR. Clinical rationale for very high field (3.0 Tesla) functional MR imaging. *Topics Magn Reson Imaging* 10 (1999): 37-50.
5. Ogawa S, Lee T-M, Kay AR, et al. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc Natl Acad Sci USA* 87 (1990): 9868-9872.
6. Ogawa S, Tank DW, Menon R, et al. Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. *Proc Natl Acad Sci USA* 89 (1992): 5951-5955.
7. Bandettini PA, Wong EC, Hinks RS, et al. Time course EPI of human brain function during task activation. *Magn Reson Med* 25 (1992): 390-397.
8. Kwong KK, Belliveau JW, Chesler DA, et al. Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation *Proc Natl Acad Sci USA* 89 (1992): 5675-5679.
9. Thulborn KR, Waterton JC, Matthews PM, et al. Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field. *Biochim Biophys Acta* 714 (1982): 265-270.
10. Thulborn KR. Clinical rationale for very high field (3.0 Tesla) functional MR imaging. *Topics Magn Reson Imaging* 10 (1999): 37-50.
11. Abduljalil AM, Kangarlu A, Burgess RE, et al. Acquisition of multislice MR images at 8 Tesla. *J Comput Assist Tomogr* 23 (1999): 335-340.

12. Ugurbil K. The road to functional imaging and ultrahigh fields. *Neuroimage* 62 (2012): 726-735.
13. FDA. Magnetom Terra 7T MRI. *Drug and Device News PT. Pharmacy & Therapeutics* 42 (2017): 726-732.
14. Thulborn KR. The Challenges of Integrating a 9.4T MR Scanner for Human Brain Imaging. In: *Ultra High Field Magnetic Resonance Imaging*. Eds Robitaille P-M, Berliner LJ, Springer Science and Business Media (2006): 105-126.
15. Vaughan JT, DelaBarre L, Snyder C, et al. 9.4T human MRI: preliminary results. *Magn Reson Med* 56 (2006): 1274-1282.
16. Erturk MA, Wu X, Eryaman Y, et al. Towards imaging the body at 10.5 Tesla. *Magn Reson Med* 77 (2017): 434-443.
17. Zaremba LA. Guidance for Industry and FDA Staff: Criteria for Significant Risk Investigations of Magnetic Resonance Diagnostic Devices. United States CDRH, FDA, and DHHS (2003).
18. Thomas BP, Welch EB, Niederhauser BD, et al. High-resolution 7T MRI of the human hippocampus in vivo. *J Magn Reson Imaging* 28 (2008): 1266-1272.
19. Thulborn KR, Lu A, Atkinson IC, et al. Quantitative sodium MR imaging and sodium bioscales for the management of brain tumors. *Neuroimag Clin N Am* 19 (2009): 615-624.
20. Atkinson IC, Thulborn KR. Feasibility of Mapping the Tissue mass corrected bioscale of cerebral metabolic rate of oxygen consumption using 17-oxygen and 23-sodium MR imaging in a Human Brain at 9.4 T. *NeuroImage* 51 (2010): 723-733.
21. Kerchner GA, Hess CP, Hammond-Rosenbluth KE, et al. Hippocampal CA1 apical neuropil atrophy in mild Alzheimer disease visualized with 7-T MRI. *Neurology* 75 (2010): 1381-1387.
22. Tallantyre EC, Morgan PS, Dixon JE, et al. 3 Tesla and 7 Tesla MRI of multiple sclerosis cortical lesions. *J Magn Reson Imaging* 32 (2010): 971-977.
23. Henry TR, Chupin M, Lehericy S, et al. Hippocampal sclerosis in temporal lobe epilepsy: findings at 7 T. *Radiology* 261 (2011): 199-209.
24. Duyn JH. The future of ultra-high field MRI and fMRI for study of the human brain. *NeuroImage* 62 (2012): 1241-1248.
25. Kangarlu A, Robitaille PL. Biological effect and health implications in magnetic resonance imaging. *Concepts in Magnetic Resonance* 12 (2000): 321-359.
26. Schenck JF. Physical interactions of static magnetic fields with living tissues. *Prog Biophys Mol Bio* 87 (2005): 185-204.
27. Ueno S and Iwasaka M: Properties of diamagnetic fluid in high gradient magnetic fields. *J App Phys* 75 (1994): 7177-7179.
28. Ueno S and Iwasaka M: Parting of water by magnetic fields. *IEEE Trans Magn* 30 (1994): 4698-4700.
29. Atkinson IC, Renteria L, Burd H, et al. Safety of human MRI at static fields above the FDA 8T guideline: Sodium imaging at 9.4T does not affect vital signs or cognitive ability. *J Magn Reson Imaging* 26 (2007): 1222-1227.

30. Atkinson IC, Sonstegaard R, Pliskin NH, et al. Vital Signs and Cognitive Function are Not Affected by 23-Sodium and 17-Oxygen MR Imaging of the Human Brain at 9.4 Tesla. J Magn Reson Imaging 32 (2010): 82-87.
31. Chakeres DW, Bornstein R, Kangarlu A. Randomized comparison of cognitive function in humans at 0 and 8 Tesla. J Magn Reson Imaging 18 (2003): 342-345.
32. Kangarlu A, Burgess RE, Zhu H, et al. Cognitive, cardiac, and physiological safety studies in ultra high field magnetic resonance imaging. Magn Reson Imaging 17 (1999): 1407-1416.
33. Chakeres DW, Kangarlu A, Boudoulas H, et al. Effect of up to 8 Tesla static magnetic field exposure on sequential human vital signs measurements. J Magn Reson Imaging 18 (2003): 346-352.
34. Patel M, Williamsom RA, Dorevitch S, et al. Pilot study investigating the effect of the static magnetic field from a 9.4-T MRI on the vestibular system. Occup Environ Med 50 (2008): 576-583.
35. Benedict RHB, Schretlen D, Groninger L, et al. Hopkins verbal learning test - revised: normative data and analysis of inter-form and test-retest reliability. Clin Neuropsychol 12 (1998): 43-55.
36. Smith A. Symbol Digit Modalities Test. Western Psychological Services, Los Angeles, CA (1991).
37. Wechsler D. Wechsler Adult Intelligence Scale. Third Edition. The Psychological Corporation, San Antonio, TX (1997).
38. Beglinger LJ, Gaydos B, Tangphao-Daniels O, et al. Practice effects and the use of alternate forms in serial neuropsychological testing. Arch Clin Neuropsychol 20 (2005): 517-529.
39. Lu A, Atkinson IC, Claiborne T, et al. Quantitative Sodium Imaging with a Flexible Twisted Projection Pulse Sequence. Magn Reson Med 63 (2010): 1583-1593.
40. Yang M, Christoforidis G, Abduljali A, et al. Vital signs investigation in subjects undergoing MR imaging at 8T. AJNR Am J Neurorad 27 (2006): 922-928.

**Citation:** Keith R. Thulborn, Ian C. Atkinson, Saad Jamil, BS, Neil H. Pliskin. Safety of 9.4 Tesla for Neuroimaging of Healthy and For-Cause Volunteers. Journal of Radiology and Clinical Imaging 2 (2019): 023-033.



This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution \(CC-BY\) license 4.0](https://creativecommons.org/licenses/by/4.0/)