Institution: University of Nottingham (UoN)

Unit of Assessment: 9

Title of case study: EMReg: Establishing the Regulatory Framework for Electromagnetic Field Exposure Limits for Magnetic Resonance Imaging

Period when the underpinning research was undertaken: 1 Jan 2000 - 31 Dec 2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by the submitting HEI:
Richard Bowtell	Professor	1987 – present
Paul Glover	Dr	2000 – present
Penny Gowland	Professor	1990 – present

Period when the impact occurred: 1 August 2013 - 31 December 2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact

The Sir Peter Mansfield Imaging Group (SPMIG) has performed fundamental research into the physiological effects of the electromagnetic fields used in Magnetic Resonance Imaging (MRI). This work has informed the development of guidelines, regulations and legislation in this area, leading to associated societal benefits. In particular our work has informed exposure guidelines for static and low frequency magnetic fields from the International Commission on Non-Ionizing Radiation Protection (ICNIRP) and the UK Health Protection Agency (HPA). In 2004 the EU Commission had issued Physical Agents Directive 2004/40/EC related to exposure to electromagnetic fields, which would have caused huge disruption of the use of MRI in Europe, had it been enforced. Our work contributed to an effort to establish that the exposure levels were over-proscriptive and based on an incorrect application of theoretical models. In 2013, this led the EU to issue a new directive 2013/35/EU, from which MRI was derogated, ensuring that the continued use of MRI remained legal. Subsequently the Health and Safety Executive (HSE) and Medicines and Healthcare products Regulatory Agency (MHRA) implemented the revised 2013/35/EU Directive into UK law and guidelines in 2016, with similar processes occurring in other EU member states. These guidelines and associated legislation referenced the Directive and the ICNIRP guidelines which were based on our work. Over the assessment period, the modifications of the Directive safeguarded the healthcare benefits of MRI for 600 million people across the EU, secured economic benefits to MRI manufacturers, and hence impacted on healthcare, public policy and the economy. In addition, our work has wider relevance to workers exposed to high magnetic fields.

2. Underpinning research

When humans are exposed to high magnetic fields they can experience sensations such as vertigo, metallic taste and visual disturbances; these can affect both the patients who have an MRI scan, and the operators who work in and around MRI scanners. We have performed a programme of research that has advanced our fundamental understanding of the physiological processes underlying these sensations. This research has exploited our expertise in electromagnetism, electronics and electrophysiology, and employed theoretical and computational modelling, along with experimental measurements. In addition to the inherent interest in this topic, a significant motivation for us to undertake this work was the installation and development of the UK's first ultra-high field (7T) MRI scanner at the School of Physics and Astronomy, University of Nottingham in 2005, since it had been suggested that such physiological effects could limit the operation of ultra-high field MRI scanners. The work involved three members of academic staff (*Bowtell, Glover*, and *Gowland*) and was underpinned by three EPSRC project grants [**i-iii**], an EPSRC/MRC Programme Grant on ultra-high field (7T) MRI [**iv**], and a Joint Infrastructure Fund award [**v**] that funded the development of the 7T scanner at the University of Nottingham. In our research we have worked across different frequency ranges of the applied magnetic fields relevant to MRI:

1) **Static Magnetic Fields and Time-Varying Magnetic Fields below 10 Hz**
We demonstrated that exposure to static magnetic fields in and around MRI scanners, including low frequency movements of the body in static fields, can produce measurable effects on the vestibular **[1-2],** taste **[3]** and visual systems. We characterised the magnetic field regimes (relative orientation, rates of change and magnitude) which produce vertigo, magneto-phosphenes and metallic taste effects. From our experiments and modelling, we verified that the Lorentz force acting on current flowing in the cupulas of the semi-circular canals in the inner ear is the dominant mechanism underlying magnetic field-induced vertigo **[1]**. Our research also provided increased understanding of the electric fields that are induced in the human body when moving in magnetic fields, and we determined a method of experimentally measuring these electric fields for the first time **[4]**.
2) **Time-Varying Magnetic Fields in the frequency range 10 Hz-100 kHz**
Time varying (~kHz) magnetic fields can induce currents in the human body, which may cause peripheral nerve stimulation (PNS). We performed numerical simulations to characterise the spatial distributions of the electric fields induced in the body by time-varying magnetic fields **[5]**. We used these results to relate applied magnetic fields, which can be readily measured, to induced current density, a parameter which is regulated in guidelines for electromagnetic exposure, but cannot easily be measured. In addition, we demonstrated a method to measure low frequency surface electric fields in humans exposed to the magnetic fields of an MRI scanner. Further, we extended the literature that had formed the basis for previous regulations, specifically measuring the effects of time-varying magnetic fields used in MRI on visual acuity and visual evoked potentials **[6]**.

3. References to the research

Publications:

[1] Mian, O.S., Li, Y., Antunes, A., **Glover**, **P.M**., Day, B.L., Effect of head pitch and roll orientations on magnetically induced vertigo, *The Journal of Physiology*, Vol. 594, Issue 4, 051-67, 2016; DOI: 10.1113/JP271513.
[2] Antunes, A., **Glover**, **P. M.,** Li, Y., Mian, O.S., Day, B. L., Magnetic field effects on the vestibular system: calculation of the pressure on the cupula due to ionic current-induced Lorentz force, *Physics in Medicine & Biology*, Vol. 57, Issue 14, 4477-87, 2012; DOI: 10.1088/0031-9155/57/14/4477.
[3] Cavin, I., **Glover**, **P. M., Bowtell, R.**, **Gowland, P.**, Thresholds for perceiving metallic taste at high magnetic field, *Journal of Magnetic Resonance Imaging*, Vol. 26, Issue 5, 1357-1361, 2007; DOI: 10.1002/jmri.21153.
[4] Sanchez, C. C., **Glover**, **P. M.,** Power, H., **Bowtell, R.**, Calculation of the electric field resulting from human body rotation in a magnetic field, *Physics in Medicine & Biology,* Vol. 57, Issue 15, 4739, 2012; DOI: 10.1088/0031-9155/57/15/4739.
[5] Bencsik, M., **Bowtell, R.,** Bowley, R.M., Electric fields induced in the human body by time-varying magnetic field gradients in MRI, *Physics in Medicine & Biology* Vol. 52, Issue 9, 2337, 2007; DOI:10.1088/0031-9155/52/9/001.
[6] **Glover, P.M**, Eldeghaidy, S., Mistry, T.R., **Gowland, P**; Measurement of visual evoked potential during and after periods of pulsed magnetic field exposure, *J. Magn. Reson. Imaging* Vol. 26, Issue 5, 1353-1356, 2007; DOI: https://doi.org/10.1002/jmri.21155.

Grants:

[i] 'Nerve stimulation due to rapidly switched magnetic field gradients in MRI', PI: Bowtell, EPSRC GR/R07899/01, (Nov 2000 - Nov 2003) GBP177,953.
[ii] 'Forward & inverse analysis of electromagnetic fields for MRI using computational mechanics techniques', PI: Jones, EPSRC GR/T22445/01, (Feb 2005 - Jan 2008) GBP208,925.
[iii] 'Measurement and modelling of electric fields induced in the human body by temporally changing magnetic fields', PI: Glover, EPSRC EP/G062692/1, (Oct 2009 - Dec 2012) GBP377,840.
[iv] 'Functional neuroimaging at ultra-high magnetic field', PI: Morris, MRC/EPSRC, Programme Grant, MRC G9900259, (Jan 2005 - Dec 2009) GBP1.8M.
[v] 'An ultra-high field facility for functional magnetic resonance', PI: Morris, Joint Infrastructure Fund, (Jan 2001 - Dec 2005) GBP2.33M.

4. Details of the impact that has occurred / is occurring to date

In 2004 the EU Commission published its Physical Agents Directive 2004/40/EC, with the aim of establishing a harmonised, legal framework for electromagnetic field (EMF) exposure of workers within the EU. This was based on guidelines issued by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) [Health Physics 74 (4):494-522; 1998]. However, the Exposure Limit Value (ELV) relating to 0-100 kHz time-varying magnetic fields (a current density of 10 mA m^{-2}) was extrapolated from very limited data and was extremely conservative. This directive, as written, would have rendered many common MRI procedures illegal, as set out in a report by the UK Health and Safety Executive (HSE) in 2007 **[a]**, and would have had a severe, negative impact on patients, health professionals, and scanner manufacturers across the whole of Europe (UK HSE report **[b]**).

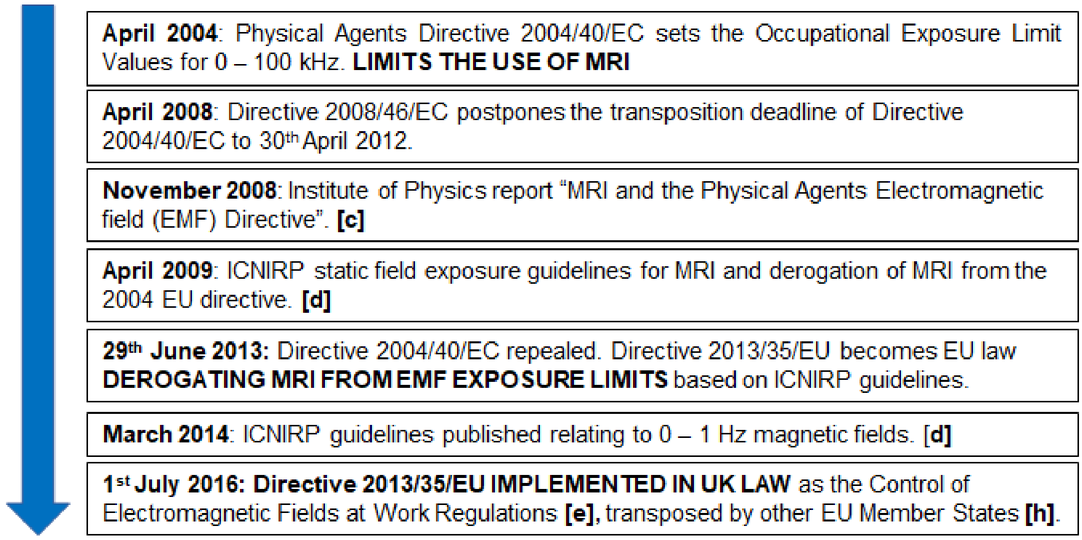

Figure 1: Timeline of the development of Directive 2013/35/EU and its transposition by the UK and other EU member states on 1st July 2016.

We recognised the limitations of the data underpinning Directive 2004/40/EC, and so performed new research to update and extend the available evidence. Our results were then used by the wider community in lobbying ICNIRP (see Institute of Physics report "MRI and the Physical Agents (EMF) Directive", 2008 **[c]**). ICNIRP then re-evaluated the underlying science, drawing extensively on our research [exemplar papers **1-6**] and produced a draft report (co-author *Gowland*) to introduce new guidelines in 2009 **[d]**. This led to Directive 2008/46/EC which postponed Directive 2004/40/EC. In June 2013, Directive 2004/40/EC was repealed and a new Directive 2013/35/EU, based on our research through updated ICNIRP 2009 guidelines, was subsequently enacted and adopted by member states in 2016.

In 2014, ICNIRP published additional guidelines relating to 0–1 Hz magnetic fields **[d]**, referencing our work: "*It is a common experience from working with clinical MR [Magnetic Resonance] imaging that vertigo sensations disappear when movement is slowed down. This indicates that there is a finite time during which the sensation of vertigo develops. In the experiment of* ***Glover et al. (2007)*** *vertigo sensations were reported by most volunteers when the duration of a single movement was less than 4 s even though there was one vertigo observation for longer duration of movement (Fig. 1)*." **[d, 2014, page 421]**. The European Commission then established a working party in 2015 (*Glover* was an expert advisor representing the European Society of Radiology), which decided that no further revision to directive 2013/35/EU was required. Directive 2013/35/EU has subsequently informed the law governing the use of MRI (and other EMF generating procedures) across the whole of Europe and was transcribed into UK law under 'The Control of Electromagnetic Fields at Work Regulations (CEMFAW) 2016' **[e]** as summarised in **Figure 1**, thus ensuring continued access to established 3T MRI scanners across the EU and in the UK.

In 2017 ICNIRP published a Statement on 'Diagnostic Devices Using Non-Ionizing Radiation: Existing Regulations and Potential Health Risks' quoting our work*:*

"Vertigo was the most frequently reported sensory side effect overall, and was more pronounced at 9.4 T than at 7 T, although its prevalence varied substantially between the different trial sites. Several mechanisms have been proposed to explain this vertigo including differences in magnetic susceptibility between the vestibular organs and surrounding fluid, induced currents acting on hair cells ***(Glover et al. 2007)*** *or the Lorentz force inside the lateral semi-circular canal (Roberts et al. 2011)."* **[d, 2017, page 314].**

Further Evidence for the Impact of our Research

1) Impact on Public Policy: Changing Underpinning Legal Frameworks

Outputs of our research [**1-7**] were incorporated into guidelines produced by several organisations. These were either: (i) introduced during the assessment period; or (ii) were effective during the assessment period having been introduced prior to August 2013. These include: the UK Health Protection Agency (2008) **[f];** ICNIRP (2009, 2014) **[d]**; the British Standards Institute and International Electrotechnical Commission (IEC) (2008) **[g]**. ICNIRP guidelines (2009, 2014), based in part on our research, have been incorporated within the legal framework for EMF exposure in Europe (population ~600M). The IEC and ICNIRP guidelines (recognised by the World Health Organisation; *Gowland* has served on its Scientific Expert Group since 2013) show the global impact of our work. These guidelines were implemented into UK law by the CEMFAW Regulations (2016) **[e]** and transposed by other EU Member States **[h]**; their enactment ensures workers and the public who are exposed to high magnetic fields in the UK, Europe and across the world, benefit from protection based on a rational and robust understanding of magnetic field exposure effects.

2) Impact on Health and Economy

The implementation of Directive 2013/35/EU and the CEMFAW 2016 regulations, based in part on our research, has mitigated a number of effects and benefitted several groups:

• Patients undergoing MRI: Directive 2013/35/EU circumvented the unnecessary restrictions which would have been enforced by Directive 2004/40/EC. These restrictions would have prevented the adoption and CE marking of 7T MRI in 2017 and prohibited further advances in ultra-high field (>7T) MRI, limited the use of 3T MRI scanners found in most large teaching hospitals, limited the use of 1.5T MRI scanners found in all hospitals **[c]**, and impacted on patients suffering from serious conditions where MRI is the leading non-invasive diagnostic technique, as well as patients requiring continual monitoring, such as those under anaesthesia and paediatric patients. The restricted use of MRI would also have increased the known risks of radiation exposure, as patients would have been subjected to alternative X-ray based imaging, particularly computerised tomography (CT). Moreover, patients would not have benefitted from the replacement of invasive procedures by interventional MRI. Overall, our research and lobbying has been critical in allowing the EU population to retain the full health benefits of mid- and high-field MRI over the assessment period.

• National Health Service (NHS): In 2016 the NHS had 405 MRI scanners, with each costing GBP721,000 on average **[i],** and 3.74 million MRI scans were performed by the NHS in 2019 **[j]**. Directive 2013/35/EU ensured that the use of this scanner infrastructure was not disrupted as a consequence of EU Directive 2004/40/EC, which would have either required costly modifications to scanners or significantly constrained their use. There are significant impacts arising from MRI's diagnostic capabilities, for example: MRI is more than twice as effective as X-ray imaging at detecting 'high genetic risk' breast cancer; MRI has improved the success rate of spinal surgery, saving the UK economy GBP166M in lost output and healthcare costs; MRI has reduced the numbers of patients with primary bone cancer who required limb amputations, saving the NHS GBP5M to GBP10M each year **[j]**.

• Manufacturers of MRI scanners: Directive 2013/35/EU, based on our research, has ensured that radical modifications to equipment and working practices to limit the EMF exposure of workers involved in the manufacture, operation and servicing of equipment, have been avoided. The MRI industry supports 2,200 UK jobs in manufacturing and GBP137M gross value added, and the global market for MRI systems was GBP4.60 billion in 2018 **[j]**. Companies outside Europe would not be affected by the guidelines, thus endangering the viability of European industry and reducing global competition.

• MRI workers: Updated MHRA guidelines (Safety Guidelines for Magnetic Resonance Imaging Equipment in Clinical Use, 2007 and DB2015 **[k]**) provide a guide to safe operation

of MRI, in line with the EU Directive/derogation, ICNIRP **[d]** and European Commission guidelines (Non-binding guide to good practice for implementing Directive 2013/35/EU, 2015 **[l]**) and HSE (HSG281: Electromagnetic fields at work: A Guide to the Control of Electromagnetic Fields at Work Regulations, 2016 **[b]**). Based on these guidelines, the Institute for Physics and Engineering in Medicine (IPEM) produced safety advice **[m]** and is now undertaking accreditation of MR Safety Experts in the UK, with *Glover* and *Gowland* contributing to the accreditation training course (delayed from Spring 2020 to Spring 2021 due to COVID-19) based on their expertise, as demonstrated in their primary papers **[n]**.
The importance of our published research **[1-6]** in providing the scientific basis for lobbying UK and EU government organisations has been confirmed in 2020 by the past-President of the Institute of Physics and Engineering in Medicine (IPEM) 2013-2015 **[o]**. *"In the ensuing campaign by the MRI community, the Nottingham group contributed in a number of ways. The group's very strong research expertise in the key areas of science meant that they were able to help explain the uncertainties and misunderstandings that had led to the data being interpreted as it had. The result of this work was that the directive was repealed in 2013 and replaced with more balanced legislation... the Nottingham group influenced the UK implementation of the directive, in the form of the Control of EMF at Work Regulations 2016, which removed the impact of the legislation on MRI in this country."*

5. Sources to corroborate the impact that has occurred:

[a] Health and Safety Executive, "Assessment of Electromagnetic Fields around Magnetic Resonance Imaging (MRI) equipment", Research Report RR570, 2007.
[b] Health and Safety Executive: "Electromagnetic fields at work. A guide to the Control of Electromagnetic Fields at Work Regulations", 2016.
[c] Institute of Physics report "MRI and the Physical Agents (EMF) Directive", 2008.
[d] ICNIRP guidelines: 2009, 2014, 2017:
2009: Vecchia, P., Matthes, R., Ziegelberger, G., Lin, J., Saunders, R., Swerdlow, A., "Exposure to high frequency electromagnetic fields, biological effects and health consequences (100 kHz-300 GHz)", (see acknowledgement page: 8).
2014: Ziegelberger, G, "ICNIRP Guidelines: For Limiting Exposure to Electric Fields Induced by Movement of the Human Body in a Static Magnetic Field and by Time-Varying Magnetic Fields Below 1 Hz." Health Physics, Vol.106 No. 3: 418-425, 2014, (see pages: 420, 421).
2017: "ICNIRP Statement: On Diagnostic Devices Using Non-Ionizing Radiation: Existing Regulations and Potential Health Risks", Health Physics, Vol. 112 No. 3: 305-321, 2017, (see pages: 305, 314, 317, 319).
[e] The Control of Electromagnetic Fields at Work (CEMFAW) Regulations, No. 588, 2016.
[f] Health Protection Agency, "Static Magnetic Fields: Report of the Independent Advisory Group on Non-ionizing Radiation", 2008 (see pages: 32, 49, 50, 65, 115, 116).
[g] British Standards Institute and International Electrotechnical Commission (IEC), "Medical Electrical Equipment, Part 2-33: Particular requirements for the safety of magnetic resonance equipment for medical diagnosis", 2008.
[h] Comparison of international policies on electromagnetic fields, National Institute for Public Health and the Environment, 2018.
[i] Magnetic Resonance Imaging (MRI) Equipment, Operations and Planning in the NHS, Clinical Imaging Board (CIB), 2017.
[j] UKRI Science and Technology Facilities Council, Case Study: STF Key in Enabling Today's High-Resolution MRI Scanners, 2020.
[k] MHRA guidelines published December 2007 and March 2015 (Safety Guidelines for Magnetic Resonance Imaging Equipment in Clinical Use).
[l] European Commission in 2015 (Non-binding guide to good practice for implementing Directive 2013/35/EU).
[m] IPEM POLICY STATEMENT: Scientific Safety Advice to Magnetic Resonance Imaging Units that Undertake Human Imaging, 8th October 2013.
[n] Letter from IPEM lead on the use of research with training guidelines (delayed from start date of Spring 2020 to Spring 2021 due to COVID-19).
[o] Letter from President of Institute of Physics and Engineering in Medicine 2013-2015.