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### Development of hypertension after long-term exposure to static magnetic fields among workers from a magnetic resonance imaging device manufacturing facility



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#### ABSTRACT

Objective: To assess the association between long-term exposure to static magnetic fields (SMF) in a magnetic resonance imaging (MRI)-manufacturing environment and hypertension.

Methods: In an occupational cohort of male workers (n=538) of an MRI-manufacturing facility, the first and last available blood pressure measurements from the facility's medical surveillance scheme were associated with modeled cumulative exposure to SMF. Exposure modeling was based on linkage of individual job histories from the facility's personnel records with a facility specific historical job exposure matrix. Hypertension was defined as a systolic pressure of above 140 mm Hg and/or a diastolic blood pressure above 90 mm Hg. Logistic regression models were used to associate cumulative SMF exposure to hypertension while adjusting for age, body mass index and blood pressure at time of first blood pressure measurement. Stratified analysis by exposure duration was performed similarly.

Results: High cumulative exposure to SMF ( $\geq 7.4\,\mathrm{K}$  Tesla minutes) was positively associated with development of hypertension (Odds Ratio [OR] 2.32, 95% confidence interval [CI] 1.27 – 4.25, P=0.006). Stratified analysis showed a stronger association for those with high cumulative SMF exposure within a period up to 10 years (OR 3.96, 95% CI 1.62 – 9.69, P=0.003), but no significant association was found for (high) cumulative exposure accumulated in a period of 10 or more years. Our findings suggest SMF exposure intensity to be more important than exposure duration for the risk of developing hypertension.

Conclusions: Our data revealed that exposure to high levels of MRI-related SMF during MRI-manufacturing might be associated with developing hypertension.

#### 1. Introduction

Magnetic Resonance Imaging (MRI) is a rapidly developing diagnostic technology with a clear trend to higher field strength scanners and increased application (Capstick et al., 2008; McRobbie, 2012). Occupational exposure to MRI scanners has been associated with self-reported health complaints and workers working with the strongest systems (1.5 and 3 T) tend to report more symptoms (Wilen and de Vocht, 2011). This underlines the importance of the assessment of health risks associated with exposure to MRI-related electromagnetic fields (EMF), including static magnetic fields (SMF). Temporary acute symptoms such as changes in postural sway (van Nierop et al., 2013), changes in visual and visuomotor performance (van Nierop et al., 2012), and neurocognitive effects (de Vocht et al., 2007a, 2006a, 2007b; de Vocht, 2007) have been associated with short-term exposure

to MRI-related SMF and time-varying magnetic fields (TvMF), among workers in MRI-production, MRI technicians and clinicians in health-care, and healthy volunteers. Hardly any data are available on health effects from long-term occupational exposure to SMF (Feychting, 2005; de Vocht et al., 2012). Available epidemiological evidence of (short and long-term) SMF exposure and long-term health effects are predominantly inconclusive due to, e.g. crude exposure assessment and small study sizes (Feychting, 2005). The need for more scientific studies, including epidemiological studies, in this area has been stressed by, among others, the World Health Organisation (van Deventer et al., 2005), the Health Council of the Netherlands (2006) and The Scientific Committee for New and Emerging Health Risk (SCENIHR) (Ahlbom et al., 2008; SCENIHR, 2015). The latter stated that at present there is a lack of adequate data (e.g human observational studies) for a proper risk assessment of occupational exposure to SMF. These institutions

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have emphasized the need for cohort studies focusing on personnel dealing with equipment that generates strong static magnetic flux densities. This is what we set out to do.

The largest groups of SMF-exposed workers (in the Netherlands) are found in clinical and research settings where MRI techniques are being applied (Schaap et al., 2013). Technicians/engineers developing and producing MRI systems, on the other hand, are presumed to have been longer, more frequently and higher exposed (Gowland, 2005), since they generally spend more time near and inside MRI scanners (of various stages of production), which are factors considered to be major determinants of exposure to SMF (Bongers et al., 2013; Fuentes et al., 2008; de Vocht et al., 2009). As part of their work, some of them will probably also have volunteered for image acquisition during the development and manufacturing of MRI scanners. Such MR-volunteer scans result not only in exposure to SMF, but also in exposure to motion induced TvMF, to pulsed time gradient magnetic fields (GMF) and radiofrequency fields (RF). The latter two exposure types are present during active scanning procedures together with exposure to acoustic noise (Bongers et al., 2017). Human and animal studies on cardiovascular effects of acute MRI-related EMF exposure have either shown no effect or indicated an effect within safety limits (Hartwig et al., 2009). Both no change in systolic and diastolic blood pressure (Sert et al., 2010) as well as a slight increase in systolic blood pressure (Chakeres and de Vocht, 2005) in humans with acute exposure have been reported. A hemodynamic compensatory mechanism to counteract the magnetohydrodynamic slowing of the blood flow has been hypothesized as a cause of the observed increase of systolic blood pressure. In addition, generation of free radicals after exposure to SMF has been suggested as a source of oxidative stress, which may lead to hypertension. The underlying mechanisms of exposure to SMF resulting in free radical generation is unclear (Okano, 2008).

The effects of long-term exposure to MRI-related EMF exposure on cardiovascular health is unknown (Hartwig et al., 2009). Here we study long-term occupational exposure to SMF and the development of hypertension in an occupational cohort of male workers of an MRI development and manufacturing facility.

#### 2. Methods

#### 2.1. Study approach and population

For this retrospective cohort study, both exposed and non-exposed current and former workers of a medical imaging device manufacturing facility in the Netherlands were selected using historical company records on employment and occupational health examinations. The base cohort was defined as all workers who had been employed at the manufacturing facility, for at least one year (365 days) between 1984 and 2010, in one or both of the business units Magnetic Resonance (MR) and X-Ray. Workers from the latter business unit were included as a reference group as workers from both business units were assumed to be similar in socioeconomic background and educational level. Workers who during their employment acted as MR-volunteers and had volunteered to undergo an MR-volunteer scan were also included in the base cohort. These groups were not mutually exclusive; part of the eligible workers had worked in both business units, and MR-volunteers worked in these two or other business units of the manufacturing facility.

Historical medical records from the manufacturing facility's health surveillance scheme were analyzed to assess whether occupational long-term exposure to SMF and/or undergoing MR-volunteer scans is associated with development of hypertension. Workers with at least two complete blood pressure measurement records were selected from the base cohort for this purpose. See Fig. 1 for a flow chart of the analytical sample selection process.

#### 2.2. Data from occupational health examinations

Data from the first and last available blood pressure measurements from the following three types of occupational health examinations (see Table 1) were used for the analyses:

- MR-related periodic occupational health examinations for certain workers of business unit MR (described below) and for workers who underwent MR-volunteer-scans.
- 2) Entry and exit occupational health examinations for workers of business unit X-ray, mandatory until 2006 to all those who were directly involved in the development or manufacturing of medical imaging devices using ionizing radiation.
- 3) Periodic occupational health examinations for workers aged 50 and up, offered on a voluntary basis every 2–4 years to all workers of the manufacturing facility aged 50 or older.

The purpose of the MR-related periodic occupational health examinations was to offer auditory testing to MRI-related acoustic noise exposed workers and to precautionary monitor the health status of SMF exposed workers. Hence, from the onset of MRI production in 1984, the manufacturing facility has provided MR-related examinations for its workers working in the vicinity of MRI systems, who were *a priori* considered to be exposed to acoustic noise and/or SMF, and for MR-volunteers. For this purpose, the manufacturing facility categorized workers working at business unit MR in three groups, based on their job title: The assumed highest exposed group was on average more than 4 h a week exposed to SMF; the lowest exposed group was less than 4 h a week exposed, but worked irregularly in the vicinity of an MRI system; and the non-exposed group that did not receive MR-related examinations.

Workers categorized as high and low exposed received an MR-related examination upon start and termination of holding an 'exposed job' at business unit MR. In addition to MR-related examinations upon start and termination, high exposed workers also received an examination every two years until the mid 90's and every three years from then onwards. MR-volunteers received MR-related examinations similar to high exposed workers; upon start of volunteering, every 2-3 years, and/or after undergoing 40 MR-volunteer scans. During an MR-related examination and before each MR-volunteer scan, MR-volunteers were screened for factors contraindicative of MRI safety, such as ferromagnetic implants, claustrophobia or discomfort during a previous MRvolunteer scan, which could exclude MR-volunteers from (temporarily) participating in the MR-volunteer program. At personal discretion of the practicing occupational physician, MR-volunteers could also be excluded from the MR-volunteer program based on results of the examination (e.g. impaired hearing or high blood pressure).

All health examinations were performed by trained occupational physicians or nurses of an external Occupational Health Service commissioned by the manufacturing facility. Aside from systolic and diastolic blood pressure measurements, we used the height and weight measurements from the examinations.

From the mid 90's data from the health examinations were entered directly into an electronic database. The paper medical records from between 1970 until the mid 90's were manually entered into the digital database between 2009 and 2010 for the purpose of our study. To account for human error during data entry, all data in the digital database were screened for anomalous values. Records with possible entry errors ( < 1%) were manually compared with the original paper records and corrected when necessary.

## 2.3. Systolic and diastolic pressure measurements and hypertension definition

Systolic and diastolic blood pressure was measured with a manual sphygmomanometer. During data-entry, the majority of analog

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