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The effect of magnetic resonance imaging on mercury release from dental amalgam at 3T and 7T

James R. Allison [a,b,c,*], Karthik Chary [c,d], Chris Ottley [e], Quoc C. Vuong [f], Matthew J. German [a,c], Justin Durham [a,b], Peter Thelwall [c,d]

[a] School of Dental Sciences, Faculty of Medical Sciences, Newcastle University, UK
[b] Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK
[c] Translational and Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, UK
[d] Centre for In Vivo Imaging, Newcastle University, Newcastle upon Tyne, UK
[e] Department of Earth Sciences, Durham University, UK
[f] Biosciences Institute, Faculty of Medical Sciences, Newcastle University, UK

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ABSTRACT

Objectives: To measure mercury release from standardised hydroxyapatite/amalgam constructs during MRI scanning and investigate the impact of static field strength and radiofrequency (RF) power on mercury release.
Methods: Amalgam was placed into 140 hydroxyapatite disks and matured for 14-days in artificial saliva. The solution was replaced, and samples split into five groups of 28 immediately prior to MRI. One group had no exposure, and the remainder were exposed to either a 3T or 7T MRI scanner, each at high and low RF power. Mercury concentration was measured by inductively coupled plasma mass spectrometry. Groups were compared using one-way ANOVA, and two-way ANOVA for main effects/ interaction of field strength/ RF power.
Results: Mercury concentration was increased in the 7T groups (high/ low: 15.43/ 11.33 ng mL^{-1}) and 3T high group (3.59) compared to control (2.44). MRI field strength significantly increased mercury release ($p < .001$) as did RF power ($p = .030$). At 3T, mercury release was 20.3 times lower than during maturation of dental amalgam, and for the average person an estimated 1.50 ng kg^{-1} of mercury might be released during one 3T investigation; this is substantially lower than the tolerable weekly intake of 4,000 ng kg^{-1}.
Conclusion: Mercury release from amalgam shows a measurable increase following MRI, and the magnitude changes with magnetic field strength and RF power. The amount of mercury released is small compared to release during amalgam maturation. Amalgam mercury release during MRI is unlikely to be clinically meaningful and highly likely to remain below safe levels.

Clinical Significance

Mercury is released from amalgam dental fillings during MRI, however the amount released is likely to be clinically insignificant and remain well below safe exposure limits.

1. Introduction

Magnetic resonance imaging (MRI) is a widely used diagnostic modality with 76 million investigations performed in 2019 in nations of the Organisation for Economic Co-operation and Development (OECD). MRI utilisation is increasing, with a 66% increase in the number of investigations performed between 2009 and 2019 [1]. One expanding area of MRI utilisation is in imaging of the head in several conditions which are more common in older patients such as stroke, dementia, and Parkinson's disease [2–4]. As the global population continues to age [5], it is therefore increasingly likely that older adults will be exposed more frequently to MRI in future.

Recent studies have reported that mercury may be released from mercury-amalgam dental restorations when exposed to MRI [6–8], thereby posing a theoretical risk of toxic effects to patients who have amalgam restorations when undergoing MRI investigations. Most

* Corresponding author at: School of Dental Sciences, Faculty of Medical Sciences, Newcastle University, Framlington Place, Newcastle Upon Tyne, NE2 4BW, UK.
E-mail address: James.allison@newcastle.ac.uk (J.R. Allison).

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previous studies of mercury release from dental amalgam have investigated field strengths of 1.5 or 3 Tesla (T) which are typically found in clinical MRI machines, however field strengths of 7T are now finding their way into clinical applications due to higher resolution and faster image acquisition [9], although this field strength is still mainly used in research settings.

The use of dental amalgam as a material for the restoration of teeth is being phased out, largely owing to concerns over environmental accumulation of mercury [10]. Despite this, amalgam is a durable material, with up to 41% of dental restorations requiring no further intervention after 15 years [11]. Dental amalgam will therefore undoubtedly be present in many patients' mouths for years to come. Given that the number of dental restorations increases with age [12], older patients with more amalgam restorations are likely to receive more MRI investigations as they age than any other generation before them.

Most authors studying the effect of MRI on mercury release from dental amalgam have proposed that the strength of the static magnetic field during MRI is likely the most significant factor, however a robust mechanism to account for mercury release has not been demonstrated. In addition to the scanner's magnetic field, radiofrequency (RF) oscillating electromagnetic fields are used to elicit an MR signal from hydrogen nuclei in body water. These fields induce eddy currents in conductive body tissues which can cause undesired heating, and scanners operate within power deposition limits (termed specific absorption rate (SAR) limits) to minimise heating risks. Some studies have demonstrated increased mercury release from amalgam following exposure to electromagnetic radiation [6,13,14]. No study has yet separately assessed the contributions of scanner static magnetic field strength and RF power deposition on mercury release from dental amalgam.

The aim of this study was to determine whether MRI causes increased mercury release *in vitro* from dental amalgam at 3T and 7T. The secondary aim was to assess the effect of scanner field strength and RF power on mercury release.

2. Methods

In this *in vitro* study, dental mercury amalgam was placed in hydroxyapatite samples and exposed to MRI. Samples were placed in artificial saliva solution and allowed to mature for 14 days before MRI exposure. Five sample groups were created, containing $n = 28$ per group. One group was not exposed to MRI scanning. The remaining four groups were split between MRI scanning at two field strengths (3T and 7T), at two RF power levels per field strength. The five experimental groups are termed 3T High, 3T Low, 7T High, 7T Low, and control. Inductively coupled plasma mass spectrometry (ICP-MS) was used to determine the mercury concentration in the artificial saliva solution following MRI exposure, and thus the quantity of mercury released from the amalgam / hydroxyapatite samples. As this study was an *in vitro* experimental study, ethical approval was not required.

2.1. Preparation of amalgam samples

5.5 mm internal diameter x 1.4 mm depth circular cavities were prepared by a single dentally trained investigator (JRA) in 140 identical 12 mm diameter x 5 mm sintered hydroxyapatite disks (Plasma Biotal Ltd; UK) using an air-turbine dental handpiece (Synea TA-98, W&H Ltd.; UK) with diamond burs (Hi-Di 525, Dentsply Sirona; PA, USA). Non-γ_2 dental amalgam (Megalloy EZ Spherical Amalgam, Dentsply Sirona; PA, USA) was triturated for 10 s using an amalgamator (Cap II Amalgamator, Henry Schein Inc.; NY, USA), and placed into the cavities in the hydroxyapatite disks. The exposed surface area of amalgam per sample was 0.238 cm^2. Samples were placed in sealed glass vessels in 8 mL of artificial saliva solution within three hours of amalgam placement (Fig. 1) and were serially allocated to one of the five groups. Following this, samples were placed in an incubator at 37 °C to mature for 14 days to allow the amalgam alloy to become stable. Samples were removed from the artificial saliva solution on the 14th day after amalgam placement, washed with deionised water, then placed into 8 mL of fresh artificial saliva in new vessels approximately 2.5 h before MRI exposure.

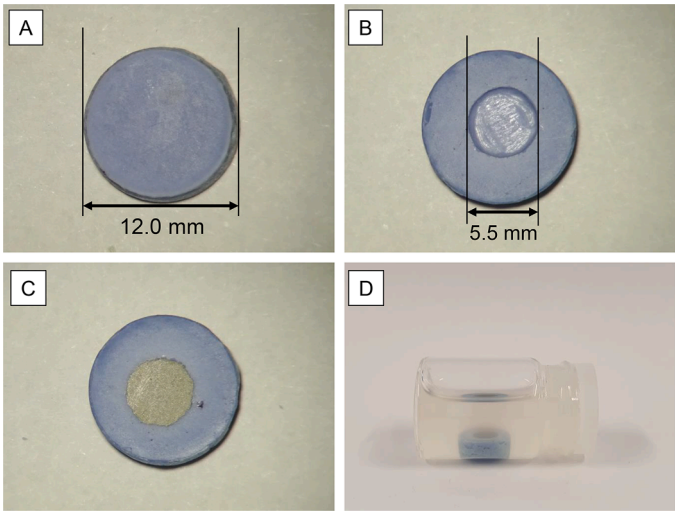

Fig. 1. Preparation of samples. A: Unprepared sintered hydroxyapatite sample; B: Sample with cavity prepared (5.5 mm diameter by 1.4 mm depth); C: Dental amalgam placed in cavity; D: Sample placed in sealed vessel containing 8 mL artificial saliva. Samples were exposed to MRI in the orientation shown in D, but were stored with the vessel in an upright orientation. In both orientations, the amalgam surface of the sample was facing upwards.

2.2. Artificial saliva

Artificial saliva solution was made up according to Earl et al. [15] by dissolving the reagents listed in Table 1 in 800 mL of deionised water using a magnetic stirrer. pH was measured using a single junction electrode (59001–82, Cole Palmer; UK) attached to a benchtop metre (Orion Star A214, Thermo Scientific; UK) and adjusted to pH 6.5 by adding 0.5 M potassium hydroxide before making up to 1 L total volume with distilled water. The solution was stored at 4 °C before use and was used within four days.

2.3. MRI protocols

Samples in the 3T High and 3T Low groups were exposed to MRI using a Philips Achieva 3T scanner (Best, The Netherlands) equipped with a quadrature body transmit coil and an 8-channel head receive array coil. Groups of 28 samples were placed within the head coil and separate, 20-minute duration pulse-acquire sequence (rectangular RF pulse shape, flip angle: 210°, B_1 amplitude: 13.5 mT) performed with a repetition time of either 33.8 ms or 169 ms for high and low SAR exposure groups respectively. Sequence timings were chosen to replicate the RF power exposure of a 20-minute neurological scan protocol at the IEC-60601–2–33 head SAR limit for the high SAR group (as determined by the scanner's SAR calculation), and at 20% of this limit for the low

Table 1
Constituents of artificial saliva. Reagents added to 800 mL distilled deionised water (DDW), pH corrected to 6.5 with 0.5 M potassium hydroxide, before making up to 1 L total volume with DDW.

Reagent	Quantity
Calcium chloride dihydrate	0.44 g
Potassium chloride	2.24 g
Potassium phosphate monobasic	1.36 g
Sodium chloride	0.76 g
Porcine stomach mucin (type 2)	2.20 g

SAR group.

Samples in the 7T High and 7T Low groups were exposed to MRI using a 7T Varian DirectDrive 31 cm diameter horizontal bore scanner (Varian Inc; Palo Alto, CA, USA) using a 72 mm quadrature birdcage volume coil (RAPID Biomedical GmBH; Germany) for RF transmission and reception. The samples in each group were scanned in batches of up to four, using a pulse-acquire sequence with a flip angle of 210° (rectangular pulse shape), a B_1 amplitude of 13.5 mT, and a repetition time of either 33.8 ms or 169 ms to form low and high SAR exposure groups respectively. The preclinical 7T scanner does not have a SAR model or per-sequence SAR calculation, so RF pulse amplitude and duration, and pulse sequence repetition time were chosen to replicate those of the 3T scans used in this study.

2.4. Mercury measurement

Samples remained in artificial saliva at 37 °C for 24 h in the sealed vessels following MRI exposure. Hydroxyapatite / amalgam samples were then removed, and the artificial saliva retained in the vessels for analysis (Fig. 2). Solutions were diluted 1:20 using 3% hydrochloric acid and then analysed using a quadrupole inductively coupled plasma mass spectrometer (ICP-MS; X-series 2, Thermo Scientific; MA, USA) to determine mercury content. Calibration was performed using an external calibration curve constructed from mercury standards of 0.00, 0.25, 0.50, 1.00, 2.00, and 5.00 ng mL^{-1}. Multiple mercury isotopes were selected for analysis: Mercury-196, −198, −199, −200, −201, and −202. Mercury-204 was not included in the analysis, due to its low natural abundance and direct Lead-204 interference. A 2 ng mL^{-1} bismuth internal standard was included in all samples and mercury standards to compensate for any matrix suppression effects in the artificial saliva matrix. Mercury measurements were also taken from a sample of the solutions in which the samples had matured for 14 days ($n = 28$ samples; maturation solution) and fresh artificial saliva solutions ($n = 6$ samples; blank solution).

2.5. Statistical methods

An *a priori* sample size calculation using G*Power (V3.1.9.7) suggested a sample size of 28 for each group for two-way ANOVA (effect size $f = 0.30$, $\alpha = 0.05$, power = 0.8, numerator df = 3), based on the lowest effect sizes reported in previous similar studies [6–8,13,14,16]. Statistical analysis and data visualisation were performed using SPSS 27 (IBM, NY, USA) and GraphPad Prism 9 (GraphPad Software Inc., CA, USA). Spearman's correlation coefficients were calculated for all analysed mercury isotopes, with associated two-tailed significance values.

One-way ANOVA was used to compare mercury concentration between all groups (Control, 3T Low, 3T High, 7T Low, 7T High), with *post hoc* Dunnett's test to compare experimental groups to the Control group. Two-way ANOVA was used in experimental groups only, to determine the main effects and interaction of MRI field strength (3T/7T) and RF power (Low/High), with two levels for each factor. Histograms and quintile-quintile plots were used to assess data distribution, and data were transformed as appropriate to meet the assumptions of two-way ANOVA (approximately normally distributed data and homogeneity of variances). Levene's test was used to assess homogeneity of variances.

3. Results

Concentrations of mercury isotopes were highly positively correlated within samples, with $0.945 \leq r \geq 0.999$ and $p < .001$ for all pairwise isotope comparisons. Mercury-202 was selected for further analysis as this is the most naturally abundant isotope of mercury. Mercury concentration was found to have a Log-normal distribution and data were therefore Log_{10}-transformed to produce an approximately normal distribution. Levene's test confirmed homogeneity of variances between groups for the transformed data, $F(4, 135) = 2.13$, $p = .081$.

Mean mercury concentration is shown in Table 2 and Fig. 3. Concentration was higher in all groups exposed to MRI compared to the control group. There was a statistically significantly difference between groups ($F(4, 135) = 72.26$, $p < .001$, $\eta^2 = 0.628$) with the 3T High ($p = .02$), 7T Low ($p < .001$), and 7T High ($p < .001$) groups exhibiting a statistically significantly higher mercury concentration than control. Both field strength ($F(1, 112) = 205.71$, $P < 0.001$, $\eta_p^2 = 0.656$) and RF power ($F(1, 112) = 4.82$, $P = 0.030$, $\eta_p^2 = 0.043$) had statistically significant effects on mercury concentration but there was no significant interaction ($F(1, 112) = 1.14$, $P = .288$, $\eta_p^2 = 0.010$).

4. Discussion

Our study demonstrated that mercury release from dental amalgam was greater following MRI scan exposure compared to control. Increasing MRI field strength and RF power both significantly increased mercury release. However, differences in hardware configuration between our 3T and 7T scanners precludes direct comparison of SAR between the field strengths used in our study. Nonetheless, measurements at 3T were performed at field strength and SAR typical of clinical

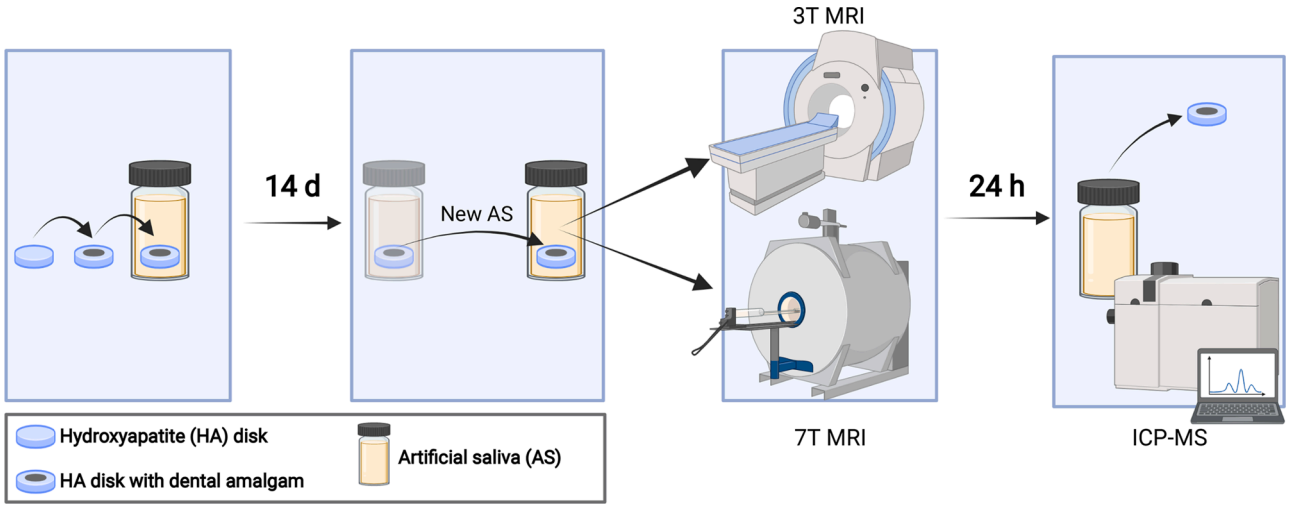

Fig. 2. Experimental design. Two groups ($n = 28$ per group) were exposed to 3T MRI at low and high Specific Absorption Rate (SAR) respectively, and the same for two groups at 7T. A fifth control group was not exposed to MRI. ICP-MS: inductively coupled plasma mass spectrometry; MRI: magnetic resonance imaging; Created using BioRender.com.

Table 2
Non-transformed mercury concentration for: experimental groups (3T Low, 3T High, 7T Low, 7T High) and Control; solution in which amalgam samples matured for 14 days prior to MRI exposure (maturation solution); and blank artificial saliva. Goemetric means are shown as data follow a log-normal distribution. Total mass of mercury released and mass released corrected for surface area of amalgam are calculated using total volume of artifical saliva (8 mL) and surface area of amalgam (0.238 cm^2).

Group (*n*)	Mean mercury concentration, ng mL^{-1}	SD	Mean total mercury released, ng	Mean mercury released corrected for surface area, ng cm^{-2}
Control (*28*)	2.44	1.56	19.55	82.27
3T Low (*28*)	3.23	1.40	25.81	108.64
3T High (*28*)	3.59	1.39	28.72	120.88
7T Low (*28*)	11.33	9.48	90.64	381.50
7T High (*28*)	15.43	13.39	123.45	519.58
Maturation solution (*28*)	72.83	103.66	582.67	2452.31
Artificial saliva (*6*)	0.20	0.60	–	–

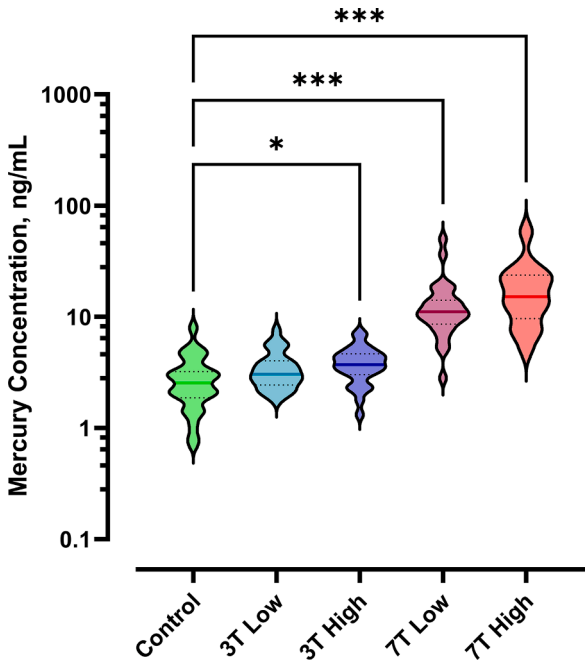

Fig. 3. Violin plot of mercury concentration in each group. Log_{10}-transformed data are plotted, however y-axis is on an antilog scale to allow presentation of the original units. Solid line shows median, and dashed lines show 1st and 3rd quartile. The width of the violins represent a kernel density estimation to show data distribution. $^*p = .02$, $^{***}p < .001$ (one-way ANOVA with *post hoc* Dunnett's test).

neurological examinations. Our data are consistent with much of the previous literature, which has variably demonstrated mercury release at field strengths of 0.23 – 3T [6–8,13,16,17], and a single study which demonstrated significant release at 7T [8]. In some of these studies, amalgam restorations had been placed much more recently (1 – 7 days) than in the present study, which may have affected the amount of mercury detected. We chose to allow the amalgam samples in this study to mature for 14 days, as the mercury release owing to the amalgamation reaction is likely to be much lower after this time as the amalgam alloy matures [18–22]. Indeed, patients are much more likely to have long-standing amalgam restorations when undergoing an MRI investigation than freshly placed ones.

Previous studies have demonstrated increased mercury release following exposure to electromagnetic radiation at various frequencies (x-ray [13], microwave [13], radio [14]) and thus, our findings replicate these earlier studies; however, the effect of RF power was modest in the present study with this factor accounting for 4.3% of the variance in the ANOVA model. Substantial effects found in other studies could again be due to the use of recently placed amalgam (< 1 day) [6,13], although one study did use samples which had matured for 14 days [14]. Our study is the first to examine the effect of increasing SAR on mercury release. A clinical scanner's SAR calculations will limit tissue power deposition to limits defined in IEC 60601–2–33, however the higher electrical conductivity of amalgam compared to tissue may elevate SAR, and thus cause heating at small length scales at the amalgam surface; this is a putative mechanism for mercury release.

In recent years there has been media interest related to concerns over mercury release from dental amalgam during MRI [23] and some professional organisations have sought to put this concern into perspective and have emphasised the need for further study [24]. Our findings suggest that increased mercury release is detectable during MRI and is affected by SAR. Crucially though, few authors have sought to understand how clinically meaningful the amount of mercury released is likely to be in comparison to safe reference ranges, or the amount of mercury released from dental amalgam during the maturation process. This is important because if the effect of MRI on mercury release is clinically meaningful, then there is a potential for harm due to mercury toxicity. However, if the effect is not clinically meaningful, either over the long or short-term, then concerns over mercury release during MRI may be unfounded. Data to help understand this problem are therefore important, as if patients are less willing to undergo MRI, avoidance of investigations may negatively impact health.

Although the use of amalgam is being phased-out internationally, recent data show that it remains a reliable and widely used restorative material, particularly in publicly-funded health systems such as in the UK [25]. Importantly, although alternatives such as resin-based composites are widely used, they possess limitations such as technique-sensitive handling characteristics, and moisture sensitivity compared to amalgam. Practitioners' confidence and experience in using these alternative materials appear to be a barrier to a rapid phase-down of amalgam [26], and it is therefore likely that amalgam will remain in the mouths of patients for many years to come.

The mean total mercury released from exposure to a 7T MRI scan at the higher RF power employed in this study (7T High group), which represents the highest mercury release observed, was 519.58 ng cm^{-2}. This is substantially lower than the total amount of mercury released during the setting and maturation of the amalgam (maturation solution), which was 2452.31 ng cm^{-2}. Based on literature showing that mercury release reaches stable levels within 14 days following trituration [18–22], and assuming that the effect of a 20-minute MRI exposure on mercury release lasts for less than 24 h, then the maximum amount of mercury liberated at the highest rate in our studies is 4.7 times lower than the amount of mercury likely to be released during amalgam maturation following placement of the restoration in the mouth, and 20.3 times lower for a 3T MRI scan at maximum SAR for the duration of the 20 min scan session. Furthermore, assuming an average of 3.7 amalgam fillings per person with an average total amalgam surface area of 0.77 cm^2 taken from Luglie et al. [27], then total mercury release from a clinically comparable, 3T MRI scan at maximum SAR would be 93.08 ng for the average person. Assuming a body mass of 62 kg [28], this would equate to 1.50 ng kg^{-1}, which is substantially lower than the European Food Safety Authority tolerable weekly intake for inorganic mercury of 4000 ng kg^{-1} body weight [29]. In fact, based on these data and assumptions, a 62 kg individual would need to have 9859 amalgam fillings to reach the tolerable weekly intake of 4000 ng kg^{-1} following a single 3T MRI scan. Alternatively, a person with average body mass and the average number of amalgam fillings would need to have 2667 3T MRI scans in one week to reach the weekly limit based on these data.

The methodology used in this study has important limitations which should be considered when interpreting the clinical relevance of the findings. Firstly, this was an *in vitro* study, and there are therefore likely to be differences compared to *in vivo* due to variation in composition and flow of saliva, exposure of amalgam to saliva in the mouth, and inhomogeneity in the MRI field due to the tissues of the body *in vivo*. An *in vitro* design however allows greater standardisation and reproducibility between samples and experimental groups. Unlike continuously flowing saliva, samples remained in the same volume of artificial saliva during MRI exposure and for 24 h after. It is likely that the concentration of mercury in real saliva is lower than in this study, as *in vivo* saliva is continuously replenished. The total amount of mercury released may however be greater *in vivo* because a higher mercury concentration in the fixed volume used in this study may reduce the mercury concentration gradient and slow the rate of release in comparison to *in vivo*. The 7T MRI machine used in this study was a preclinical scanner, without a clinically relevant SAR calculation, rather than a scanner with regulatory approval for diagnostic imaging as was used for 3T groups. Comparability of the results between the 3T and 7T scanners is based on reproduction of B1 amplitude, RF pulse duration and RF pulse duty cycle, rather than operation within the SAR limit of a 7T clinical MRI scanner. As mercury concentration was measured at a single timepoint (24 h) after MRI we have no data on the time course of mercury release from amalgam. To address these limitations, future studies should aim to longitudinally measure mercury in clinical samples, such as in saliva, during MRI in human participants.

In conclusion, the release of mercury from dental amalgam occurs during MRI and is affected by the RF power deposition (SAR level) of the scan and likely also the field strength. However, the amount of mercury released is very unlikely to be clinically meaningful and is likely to remain well below safe intake levels. The release of mercury from dental amalgam should therefore not be a clinically meaningful concern during MRI examinations, even for patients with many amalgam fillings.

Credit author statement

JRA contributed to conception, design, data acquisition and interpretation, drafted and critically revised the manuscript. KC contributed to data acquisition and critically revised the manuscript. CO contributed to design, data acquisition and interpretation, and critically revised the manuscript. QCV contributed to conception, design, and critically revised the manuscript. MJG contributed to design, data interpretation, and critically revised the manuscript. JD contributed to conception, design, and critically revised the manuscript. PT contributed to, design, data acquisition and interpretation, and critically revised the manuscript. All authors gave their final approval and agree to be accountable for all aspects of the work.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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