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Ex Vivo Mercury Release from Dental Amalgam after 7.0-T and 1.5-T MRI

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Purpose: To evaluate ex vivo mercury release from dental amalgam after 7.0-T and 1.5-T MRI.

Materials and Methods: The authors evaluated 60 caries-free molar or premolar teeth that had been extracted for clinical indications. Two-sided cavities were opened in each tooth and amalgam fillings applied. After 9 days, two groups of 20 randomly selected teeth were placed in 20 mL of artificial saliva immediately followed by 20 minutes of MRI exposure at 1.5 or 7.0 T. A control group of teeth was placed in artificial saliva without undergoing MRI exposure. The teeth were removed from the artificial saliva 24 hours later, and the saliva was analyzed for mercury content by using inductively coupled plasma mass spectrometry. One-way analysis of variance was used to compare the mean mercury values among the three independent groups, and the Tukey test was used for multiple comparisons of the mean values.

Results: The mean mercury content of the artificial saliva was 673 μg/L ± 179 in the 7.0-T MRI group, 172 μg/L ± 60 in the 1.5-T MRI group, and 141 μg/L ± 152 in the control group. The mercury content in the 7.0-T group was greater than that in both the 1.5-T group ($P < .001$; 95% confidence interval: 368 μg/L, 633 μg/L) and the control group ($P < .001$; 95% confidence interval: 416 μg/L, 648 μg/L). There was no statistically significant difference in mercury content between the 1.5-T and control groups ($P = .84$; 95% confidence interval: −164 μg/L, 110 μg/L).

Conclusion: In an ex vivo setting, mercury was released from amalgam fillings after exposure to 7.0-T MRI but not 1.5-T MRI.

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The use of dental amalgam fillings remains popular despite the controversy surrounding its potential effects on human health (1–4). The American Dental Association has reported that 100 million amalgam filling procedures are performed every year in the United States (5). However, since 2008, the use of amalgam fillings has been forbidden or restricted in Sweden, Norway, Denmark, and Germany (1). In addition, the European Parliament has adopted a ban on the use of amalgam in clinical practice for children younger than 15 years and pregnant or lactating women, effective by 2018.

The oropharyngeal region is an area in which metals are often used for dental applications. These dental materials often contain precious (gold, silver, platinum) and nonprecious (chromium, cobalt, molybdenum, nickle) metals, amalgam, pure gold, titanium, and titanium alloys (6,7). Dental implants and surgical reconstruction materials are mostly made of titanium, stainless steel, and vitallium (7). Studies that are conducted to characterize the MRI properties of these materials for patient safety purposes use in vitro testing methods (7,8). Dental amalgam has been in use for the past 200 years and consists of approximately 50% mercury. The release of mercury from amalgam fillings occurs through metal ions (mercury ions) and evaporation of mercury (elemental). Various conditions that occur during and after the restoration process, such as chewing, brushing, and corrosion, result in mercury discharge. Although approximately 40% of the mercury released from amalgam passes into the saliva in the form of metal ions and enters the gastrointestinal system (10% is absorbed), 60% is released as mercury vapor and is either inhaled and enters the circulation in the lungs or is exhaled. It has been suggested that release of mercury into the environment during the application or removal of amalgam may also have some potentially detrimental effects on the body (2,9).

Several previous studies have examined amalgam-filled teeth in terms of translational interaction, heating rates, and microleakage after MRI (8,10,11). To our knowledge, no previous study has tested the effects of 7.0-T MRI on mercury release from amalgam fillings, and we hypothesized that 7.0-T MRI can trigger mercury release. The aim of this study was to investigate the mercury release into artificial saliva from amalgam-filled teeth exposed to 7.0-T and 1.5-T MRI in an ex vivo setting.

Materials and Methods

This study was approved by the Kirikkale University Clinical Research Ethics Committee. Written informed consent was obtained from patients for the use of extracted teeth in this project.

Sample Preparation

Human teeth that had been extracted for various reasons (eg, orthodontic procedures, third-molar extractions, and periodontal hypermobility) were used for this study. The study included 60 caries-free molar or

Summary

Nine days after dental restoration, exposure to 7.0-T MRI was associated with mercury release from dental amalgam in an ex vivo experimental setting.

Implications for Patient Care

- Nine days after restoration of human teeth with dental amalgam containing mercury, exposure to 7.0-T MRI was associated with mercury release in artificial saliva in an ex vivo setting.
- In the same ex vivo setting, no mercury release was observed after exposure of amalgam-restored teeth to 1.5-T MRI.
- Further studies of mercury amalgam at 7.0-T MRI may be warranted to evaluate the relationship between high-field-strength MRI and release of mercury from dental amalgam.

premolar teeth that were kept in disinfectant solution and stored in an isotonic saline solution for no longer than 3 months after extraction. Following surface débridement, each tooth was prepared by using dental pumice and rubber mill, operated by a specialist in restorative dentistry. Two-sided cavities were opened in each tooth by using diamond burrs and aerators, and amalgam fillings were placed under standard conditions (Fig 1). All samples were burnished with cotton pellets to remove residual mercury from their surface. The 60 teeth were randomly selected and divided into three groups of 20 each. One group underwent 7.0-T MRI, one group underwent 1.5-T MRI, and one group did not undergo MRI (control group).

All teeth were evaluated 9 days after the dental filling procedure. Immediately before MRI, the teeth were placed in Plexiglas test tubes containing 20 mL of artificial saliva (Fusayama/Meyer Artificial Saliva; Pickering Laboratories, Mountain View, Calif) (Fig 2).

7.0-T MRI Group

MRI was performed with a 7.0-T MR unit (Magnetom Trio; Siemens Healthineers, Erlangen, Germany) by applying a head imaging protocol (axial T1-weighted thin-section imaging before and after the administration of contrast material, axial T1- and T2-weighted fast spin-echo imaging, T1-weighted imaging, magnetization-prepared rapid acquisition gradient-echo imaging, T2-weighted imaging, T2-weighted fluid-attenuated inversion-recovery imaging, and T2-weighted coronal and sagittal fast spin-echo imaging) with a head coil (Nova 1Tx/32Rx, Siemens Healthineers) and exposure to a static and varying magnetic field for approximately 20 minutes. Twenty-four hours after imaging, the teeth were removed from the tubes and the artificial saliva was stored in a closed container for analysis.

1.5-T MRI Group

A 1.5-T MR unit (Achieva; Philips Medical Systems, the Netherlands) was used to perform MRI for approximately 20 minutes with the same protocol used for 7.0-T imaging. Twenty-four hours after imaging, the teeth were removed from the tubes and the artificial saliva was stored in a closed container for analysis.

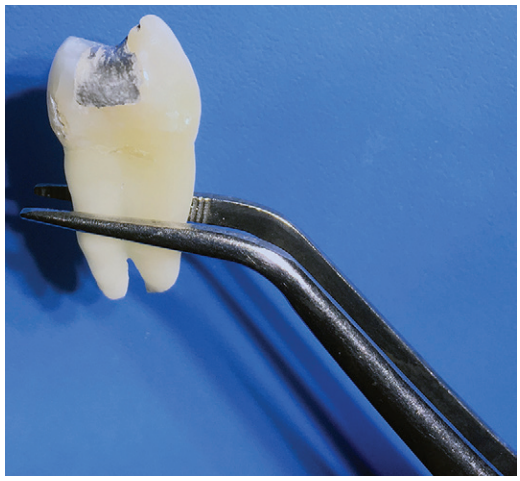


Figure 1: Sample tooth with amalgam filling routinely used in clinical practice.

Control Group

The teeth in the control group were placed into artificial saliva 9 days after the fillings were placed. After 24 hours, the teeth were removed from the tubes and the artificial saliva was stored in a closed container for analysis.

Mercury Concentration Analysis

To determine the concentration of mercury in the artificial saliva, inductively coupled plasma mass spectrometry (Spectro Analytical Instruments, Kleve, Germany) was performed in the Kirikkale University Central Research Laboratories. The sample tubes were numbered, and the laboratory technician was not aware of group assignment. Three separate 0.5-mL samples were obtained from the 20-mL artificial saliva within the tubes. The mean mercury values from the three analyses were used for statistical comparison.

Statistical Methods

The power analysis was performed with software (G*power, version 3.1.9.2; developed by Franz Faul, Universität Kiel, Germany) and indicated that a total sample size of 60 subjects would provide greater than 88% power (actual power = 0.88) to detect significant differences with an effect size of 0.40 at α of .05. Mean mercury values were determined with 95% confidence intervals. A one-way analysis of variance test was used to compare the mean mercury values among the three independent groups. The Tukey test was used for multiple comparisons of the mean values among the groups. Descriptive statistics were expressed as means ± standard deviations for numeric variables. Software (SPSS for Windows, version 24.0; IBM, Armonk, NY) was used for statistical analysis, and $P < .05$ was considered to indicate a statistically significant difference.

Results

The mean mercury values were 673 μg/L ± 180 in the 7.0-T MRI group, 172 μg/L ± 60 in the 1.5-T MRI group, and 141 μg/L ± 152 in the control group (Fig 3). One-way analysis of variance revealed a statistically significant difference in mean mercury values among the three groups ($P < .001$) (Table).

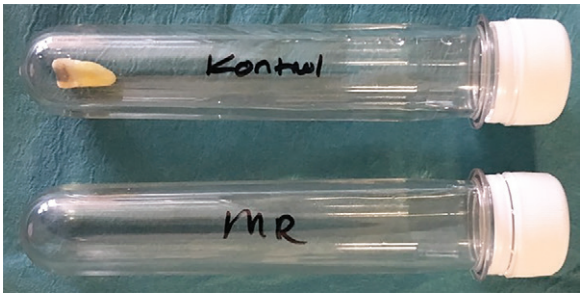


Figure 2: Sample tubes containing, top, tooth with dental amalgam in artificial saliva in preparation for testing and, bottom, artificial saliva only. Tube had previously undergone MRI, and the tooth was removed 24 hours after imaging.

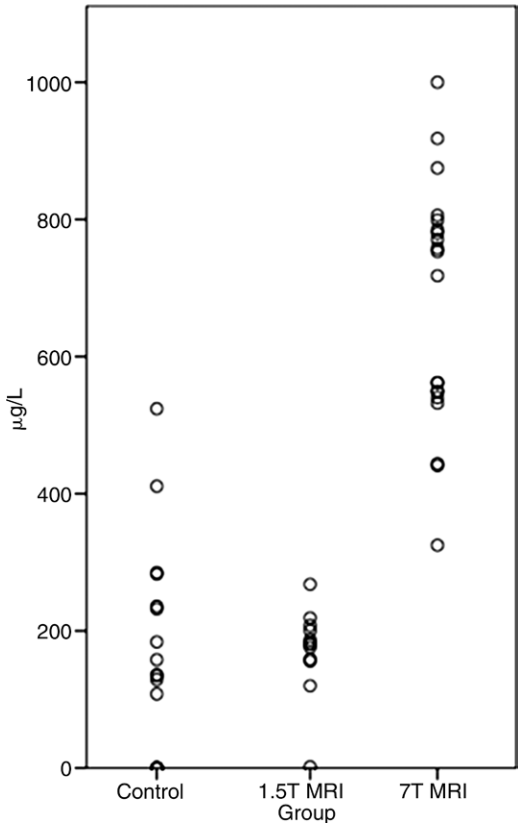


Figure 3: Beeswarm plot shows mercury content in artificial saliva of the three groups. Mean mercury values of artificial saliva were 673 μg/L ± 180 in 7.0-T MRI group, 172 μg/L ± 60 in 1.5-T MRI group, and 141 μg/L ± 150 in control group.

According to the Tukey multiple comparison test, the mercury content in the 7.0-T group was significantly greater than that in both the 1.5-T group ($P < .001$; 95% confidence interval: 368 μg/L, 633 μg/L) and the control group ($P < .001$; 95% confidence interval: 416 μg/L, 648 μg/L). However, there was no statistically significant difference in mercury content levels between the 1.5-T and control groups ($P = .84$; 95% confidence interval: −164 μg/L, 110 μg/L).

Discussion

In our study, the mean mercury concentrations released into artificial saliva from amalgam fillings 24 hours after 7.0- and 1.5-T MRI were 673 μg/L and 172 μg/L, respectively. We concluded that, 9 days after dental restoration, exposure to 7.0-T MRI was associated with mercury release from dental amalgam in an ex vivo experimental setting.

In the literature, two studies examined the effects of MRI on dental amalgam fillings (12,13). The first study, performed in 1996 by Müller-Miny et al (12), used 1.5-T MRI. They exposed amalgam-filled dental models to a static magnetic field for 24 hours and to a gradient-echo sequence for 60 minutes. In both situations, they found no significant increase in mercury levels (maximum level, 2.5 μg/L mercury). In the second study, performed in 2014, Kursun et al (13) carried out a temporomandibular joint MRI protocol at 1.5 T and exposed amalgam disks to the magnetic field for approximately 30 minutes. They reported that MRI had no effect on mercury release from dental amalgam (mean, 9.1 μg/L mercury). In the current study, we observed higher levels of mercury in the 1.5-T group (mean, 172 μg/L mercury). Differences in absolute levels of mercury may depend on the age of the amalgam and the conditions of its preparation. The samples in our study were not stored in routinely refreshed saline solution, which may cause corrosion and reduce the amount of mercury in the filling material. Our samples were stored in dry, closed boxes until imaging.

After trituration and insertion of amalgam into a patient's tooth, mercury continues to release while setting (hardening or amalgamation) for 48 hours. After completion of the amalgamation, the main source of mercury is the matrix in the γ-1 phase. Over time, this phase gradually transforms into the β-1 phase, which contains less mercury, and this conversion causes the release of mercury (14). In addition to this sustained mercury release, other factors affecting the release process include dismantling of the filling, wear from mechanical stimuli (chewing, consumption of carbonated drinks, functional movements such as brushing of the teeth, and parafunctional habits such as bruxism), galvanic corrosion, electrochemical corrosion, and oral conditions (temperature, pH level, and negative air pressure) (3,4,15,16). Previous studies have measured the amounts of mercury released due to these factors (5,17–19). The World Health Organization estimates that the daily absorbed dose from amalgam is 122 μg mercury, and the Environmental Protection Agency provides a reference concentration of 0.3 $\mu g/m^3$ for inhalation. In the present study, the dissolved amount of mercury was observed to be in the range of 325–1000 μg/L mercury after 7.0-T MRI. An important point of discrimination concerning safety and hazard to human health is the amount of mercury that is absorbed by the vital tissues.

In a set amalgam, phase transformation is accelerated by an increase in temperature (20). The details of this transformation phenomenon are not completely understood (21,22). We believe that the mercury release after 7.0-T MRI might be caused by phase changes stimulated by high-field-strength imaging. Studies examining the effect of the magnetic field on alloys have shown that high magnetic fields have an effect on phase transformation, recrystallization, and particle structure distribution

Comparison of Mercury Content in Artificial Saliva according to Group

Group Comparisons	Mean Mercury Value (μg/L)	Mean Difference (μg/L)	Standard Error	*P* Value	95% Confidence Interval (μg/L)
Control group	141	...	…	…	…
Versus 1.5-T MRI group	172	−27	56.8	.84	−164, 110
Versus 7.0-T MRI group	673	−533*	47.8	<.001	−648, −416
1.5-T MRI group	172	…	…	…	…
Versus control group	141	27	56.8	.84	−110, 164
Versus 7.0-T MRI group	673	−506*	56.8	<.001	−633, −368
7.0-T MRI group	673	…	…	…	…
Versus control group	141	533*	47.8	<.001	416, 648
Versus 1.5-T MRI group	172	506*	56.8	<.001	368, 633

* The mean difference is significant at the $P < .05$ level.

(23,24). In these studies, the effects of a magnetic field up to19–30 T were investigated with various metallic alloys. In 2016, Alkurt et al (25) studied devices that used magnetic fields of 0.2 and 1.5 T and did not detect any phase change in the dental amalgam. The amalgam currently used in clinical practice is a metallurgically complex biomaterial. Thorough analysis and understanding of these phase characteristics and corrosion reactions are important for both the clinical effectiveness of the amalgam and the detection of adverse biologic effects.

Another possible cause of mercury release is electrochemical corrosion. When the surface of an alloy comes into contact with aqueous media, an electrical potential emerges. Electrochemical corrosion, which can be seen in almost every region of hardened amalgam, is caused by the reaction with chemicals in the liquid medium, resulting in soluble and insoluble corrosion products. Dental amalgam is a dynamic and complex biomaterial, and solid-state reactions continue for a long time (20). The composition of saliva, the presence of different kinds of metals in the mouth, and high temperatures can provide a favorable environment for corrosion.

The amalgam becomes a high-temperature metallurgic system when the temperature inside the mouth reaches 75% of the γ-1 phase melting point. Tsutsumi et al (26) studied the thermal behavior of dental amalgams at temperatures of 25°–130°C and concluded that the phase transformation occurred at approximately 100°C in high-copper amalgams. They reported that, despite high temperatures, mercury release was reduced by an oxide film formed on the amalgam. Ferracane et al (27) observed mercury release from four different types of dental amalgams at temperatures of 37°C, 80°C, and 110°C for a period of 4 hours. They found that the evaporation rate was essentially independent of temperature for three types of amalgam, and that one type demonstrated a thermal link with mercury release. In addition, controversy exists surrounding the role of hot liquids in the mouth in the release of mercury (18,28). In our experiments, the 7.0-T MRI devices were operated within limits of the specific absorption rate for imaging of the head, but we did not assess the heating of amalgam under these conditions.

The safety of dental implants and metals in the maxillofacial region has been studied with 7.0-T devices (29–31). Dula et al (29) tested 28 implants and foreign bodies inside the head and reported that eight of the objects determined to be safe for 3.0-T MRI posed a potential risk for 7.0-T MRI. In 2014, Oriso et al (30) studied full-metal crowns, attachment holders, implants, and abutments with a 7.0-T MRI device in terms of warming and observed a significantly higher deflection angle of the materials with the 7.0-T device than with the 3.0-T device. In the same study, they found a temperature increase of 0.2°–0.8°C in dental restorations. However, the dental restorations were composed of alloys of gold, platinum-gold, silver, cobalt-chromium, and nickel-chromium that are used in full-metal crowns.

At present, one limitation of our study is that we do not know whether a heat build-up occurs in amalgam fillings due to various MRI procedures. Another limitation is that the artificial saliva samples were analyzed only once (after 24 hours); therefore, the change in release pattern over time was not evaluated. In our study, we treated each tooth with double-sided amalgam restorations (mesio-occlusal/disto-occlusal), which are commonly used in clinical practice. We did not perform the burnishing and polishing steps. In one of the fillings, that lack of polishing, which is normally performed in clinics to reduce corrosion, may have caused some increase in mercury release. Finally, this demonstration was conducted in an ex vivo experimental setting, without the benefit of data on the patient-specific absorption rates of mercury.

In conclusion, the results of our study indicated that 7.0-T MRI (but not 1.5-T MRI) is associated with mercury release 9 days after placement of dental amalgam fillings in ex vivo human teeth. Further studies of mercury amalgam with 7.0-T MRI may be warranted to evaluate the relationship between high-field-strength MRI and release of mercury from dental amalgam.

Author contributions: Guarantors of integrity of entire study, S.Y., M.Z.A.; study concepts/study design or data acquisition or data analysis/interpretation, S.Y., M.Z.A.; manuscript drafting or manuscript revision for important intellectual content, S.Y., M.Z.A.; approval of final version of submitted manuscript, S.Y., M.Z.A.; agrees to ensure any questions related to the work are appropriately resolved, S.Y., M.Z.A.; literature research, S.Y., M.Z.A.; clinical studies, S.Y.; experimental studies, S.Y.; and manuscript editing, S.Y., M.Z.A.

Disclosures of Conflicts of Interest: **S.Y.** disclosed no relevant relationships. **M.Z.A.** disclosed no relevant relationships.

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Radiology

Letters to the Editor

Diffusion-weighted MRI in Multicenter Trials of Breast Cancer

From
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Editor:

We greatly appreciated the insightful commentary by Dr Nandita M. deSouza (1) on our recent article reporting results of American College of Radiology Imaging Network (ACRIN) trial 6698, a multicenter trial investigating diffusion-weighted (DW) MRI for monitoring breast cancer response to therapy (2). Dr deSouza accurately described a number of important challenges and pitfalls of implementing DW MRI in multicenter trials and in utilizing the apparent diffusion coefficient (ADC) as an imaging biomarker to monitor therapy, in particular emphasizing the need for rigorous quality control and standardization measures (1).

Specifically, Dr deSouza stated: "The inclusion of test-retest studies in multicenter trials using quantitative imaging biomarkers is invaluable….The use of a test-retest approach in the I-SPY 2 trial would have confirmed the validity of the ADC changes…." and "The I-SPY 2 [Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging and Molecular Analysis 2] trial has been a marathon multicenter undertaking….However, future trials must incorporate rigorous quality assurance, quality control, and reproducibility measures to both data acquisition and processing when treatment decisions are proposed based on interpretation of quantified parameter changes such as ADC."

We heartily agree and would therefore like to respectfully point out that the ACRIN 6698 trial did in fact include a secondary aim to perform a test-retest ADC repeatability substudy. We regret that space limitations did not allow us to include this information along with the primary analysis in our article, and so Dr deSouza was not aware of the test-retest study at the time of her commentary. However, we have since published the ACRIN 6698 test-retest study results (3) and would like to make the readers aware of that additional information, which may be helpful for interpreting results of the study and in planning future trials incorporating quantitative breast DW imaging. In the ACRIN 6698 test-retest study, a coffee-break design was used to assess variability between repeat DW images, and both intra- and interreader agreement in tumor ADC quantitation were assessed. Overall, the results showed that excellent repeatability and reproducibility of breast tumor ADC measures could be achieved in a multi-institution setting using a standardized protocol and quality assurance procedure, but also supported the need for ongoing quality control methods to ensure consistent image quality and reduce data loss.

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Erratum

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Ex Vivo Mercury Release from Dental Amalgam after 7.0-T and 1.5-T MRI

Selmi Yilmaz, M. Zahit Adisen

Erratum in:
Radiology 2019;291(2):546
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The incorrect trade name was given for the 7.0-T MRI unit. "Magnetom Trio" should be "**Magnetom.**"

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