

# Prognos<sup>®</sup> in the Diagnosis of Amalgam Hypersensitivity – a Diagnostic Case-Control Study

Wolfgang Köhler<sup>a</sup> Klaus Linde<sup>a</sup> Stefan Halbach<sup>b</sup> Thomas Zilker<sup>c</sup> Leo Kremers<sup>d</sup>  
Reinhard Saller<sup>e</sup> Dieter Melchart<sup>a, e</sup>

<sup>a</sup>Centre for Complementary Medicine Research, <sup>b</sup>Division of Clinical Toxicology, Department of Internal Medicine II, Technische Universität München,

<sup>c</sup>Institute of Toxicology, GSF – Research Center for Environment and Health, Oberschleißheim,

<sup>d</sup>School of Dentistry, Ludwig-Maximilians-Universität München, Germany

<sup>e</sup>Division of Complementary Medicine, Department of Internal Medicine, Universitätsspital Zürich, Switzerland

## Key Words

Prognos<sup>®</sup> · Electroacupuncture · Complementary medicine · Dental amalgam · Adverse effects · Mercury

## Summary

**Objective:** We aimed to investigate whether the Prognos<sup>®</sup> device might be a useful tool in the diagnosis of disorders suspected to be due to dental amalgam fillings. **Participants and Methods:** A diagnostic case-control study was performed in 27 patients who complained about health problems attributed to amalgam (cases), 27 healthy volunteers with amalgam fillings (controls I), and 27 healthy amalgam-free volunteers (controls II). All participants were tested before and after application of 300 mg DMPS (2,3-dimercapto-1-propanesulfonic acid) with Prognos<sup>®</sup>, a diagnostic device for the energetic measurement of Traditional Chinese Medicine meridians. In addition, mercury was measured in blood, urine, and saliva, and a lymphocyte transformation test (LTT) was performed. **Results:** Diagnoses derived from the first and second Prognos<sup>®</sup> testing did not agree above chance (Cohen's Kappa = -0.11, 95% confidence interval -0.33 to 0.10;  $p = 0.30$ ). Agreement for secondary outcome measures was poor, too. Prognos<sup>®</sup> measurements did not differ between cases and controls. Correlations with measurements in urine, blood and saliva were low. **Conclusion:** In this study Prognos<sup>®</sup> could not be shown to be a useful tool in the diagnosis of disorders suspected to be due to dental amalgam fillings.

## Schlüsselwörter

Prognos<sup>®</sup> · Elektroakupunktur · Komplementärmedizin · Amalgam · Nebenwirkungen · Quecksilber

## Zusammenfassung

*Prognos<sup>®</sup> in der Diagnose einer Amalgam-Überempfindlichkeit – eine diagnostische Fall-Kontroll-Studie*

**Fragestellung:** In dieser Studie sollte untersucht werden, ob das Prognos<sup>®</sup>-Messgerät ein geeignetes diagnostisches Instrument beim Verdacht auf amalgambedingte Erkrankungen ist. **Teilnehmer und Methoden:** Eine diagnostische Fall-Kontroll-Studie wurde an 27 Patienten, die ihre gesundheitlichen Beschwerden auf Amalgamfüllungen zurückführten (Fälle), 27 gesunden Amalgamträgern (Kontrollgruppe I) und 27 gesunden amalgamfreien Teilnehmern (Kontrollgruppe II) durchgeführt. Alle Teilnehmer wurden jeweils vor und nach Einnahme von 300 mg DMPS (2,3-Dimercapto-1-Propansulfonsäure) mit dem Prognos<sup>®</sup>-Messgerät, das den Energiezustand der Meridiane gemäß der Traditionellen Chinesischen Medizin misst, untersucht. Weiterhin wurden Quecksilber in Blut, Urin und Speichel gemessen sowie ein Lymphozytentransformationstest (LTT) durchgeführt. **Ergebnisse:** Die Diagnosen der ersten und zweiten Prognos<sup>®</sup>-Messung stimmten nicht überzufällig überein (Cohens Kappa = -0,11, 95%-Konfidenzintervall -0,33 bis 0,10;  $p = 0,30$ ). Die Reliabilität der Ergebnisse der Einzelsubstanzmessungen war ebenfalls gering. Die Ergebnisse der Prognos<sup>®</sup>-Messungen unterschieden sich nicht signifikant zwischen Beschwerdeträgern und Kontrollen. Die Ergebnisse der Prognos<sup>®</sup>-Messungen korrelierten nicht oder nur in geringem Ausmaß mit denen der Messungen in Urin, Blut und Speichel. **Schlussfolgerung:** Die Ergebnisse der vorliegenden Studie sprechen nicht dafür, dass das Prognos<sup>®</sup>-Testgerät für die Diagnostik von vermutlich amalgambedingten Beschwerden geeignet ist.

## Introduction

There is considerable discussion whether amalgam dental fillings can cause diseases or not. So far there is no convincing evidence from epidemiological, toxicological or immunological research that ‘amalgam burden’ or ‘amalgam hypersensitivity’ (beyond rare cases of proven allergic reactions like oral lichenoid reactions) are valid pathological concepts [1, 2]. Nevertheless many patients and physicians are convinced that amalgam is hazardous to health [3, 4].

In 1996, a group of about 1,500 patients who attributed their chronic complaints to amalgam fillings filed a lawsuit against Degussa, the major German manufacturer of this material. A settlement was reached in which the manufacturer agreed to sponsor an independent research program (German Amalgam Trial = GAT) which was administrated by an independent research funding body (Stifterverband für die Deutsche Wissenschaft). Several studies were performed to investigate (a) the risks associated with dental amalgam fillings; (b) diagnostic procedures possibly adequate to verify amalgam hypersensitivity; (c) potential therapies. The study on hand is focusing on common diagnostic methods to investigate a possible amalgam burden.

A device frequently used by practitioners of complementary and alternative medicine is the Prognos<sup>®</sup> instrument. The device was originally developed for the Russian space program to monitor the health status of cosmonauts and, if necessary, to intervene therapeutically [5]. On the diagnostic level, Prognos<sup>®</sup> aims to provide a comprehensive energetic assessment within the framework of Traditional Chinese Medicine (TCM) concepts. The electric skin resistance at terminal meridian points at fingers and toes is measured [6, 7]. Using a software program a variety of findings on the energetic status of meridians and the organism is derived. We investigated (1) whether there is agreement between the diagnostic findings of the Prognos<sup>®</sup> device related to amalgam hypersensitivity obtained at two separate sessions; (2) whether they correlate with other tests used in the diagnosis of amalgam hypersensitivity; (3) whether the findings of Prognos<sup>®</sup> and other diagnostic tests differ between patients with suspected amalgam hypersensitivity, healthy amalgam bearers, and healthy amalgam-free volunteers.

## Methods

### Design and Participants

The study used a case-control design with two control groups. Group 1 consisted of 27 patients (cases) fulfilling the following criteria: symptoms attributed (by patients and/or care providers) to amalgam fillings;  $\geq 10$  symptoms ( $\geq 3$  with severe intensity) from a list of 50 symptoms (with a rating scale of 0 = not present to 3 = severe; single items were added to a symptom score), commonly reported by patients with amalgam hypersensitivity [8];  $\geq 5$  amalgam surfaces; age 20–65 years. All patients underwent a thorough medical examination to rule out relevant comorbidity. Group 2 (healthy amalgam bearers, controls I) consisted of 27 healthy (according

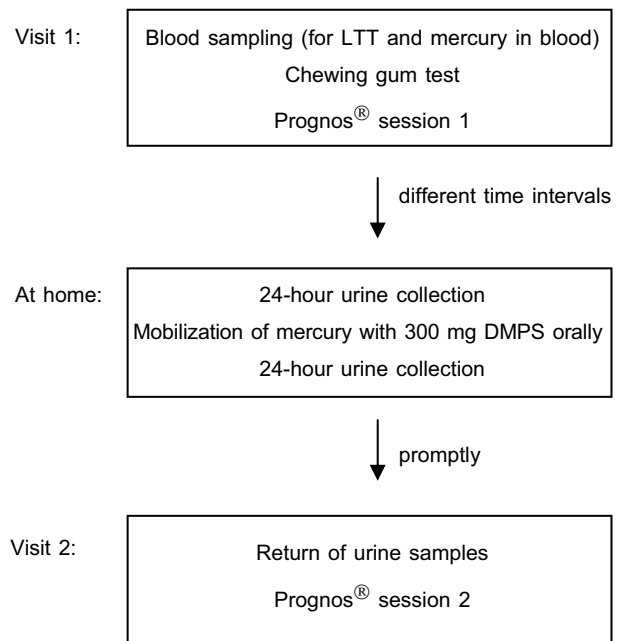


Fig. 1. Flow chart of testings.

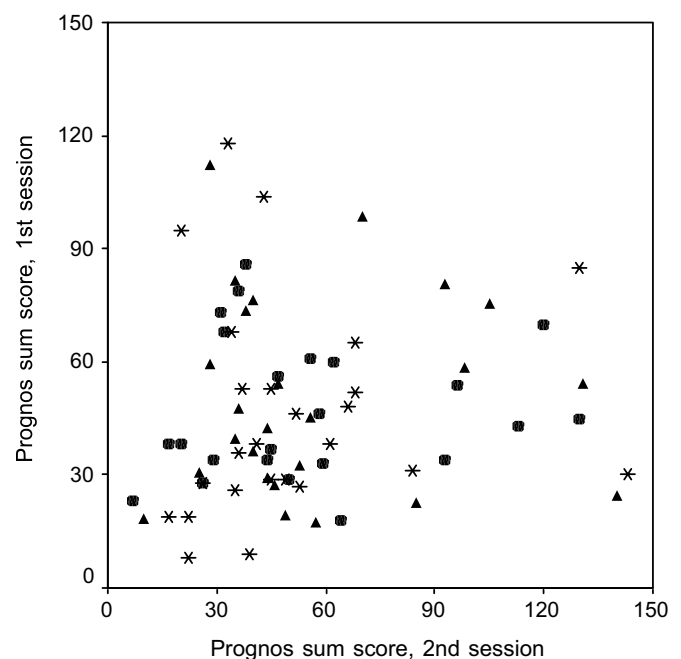
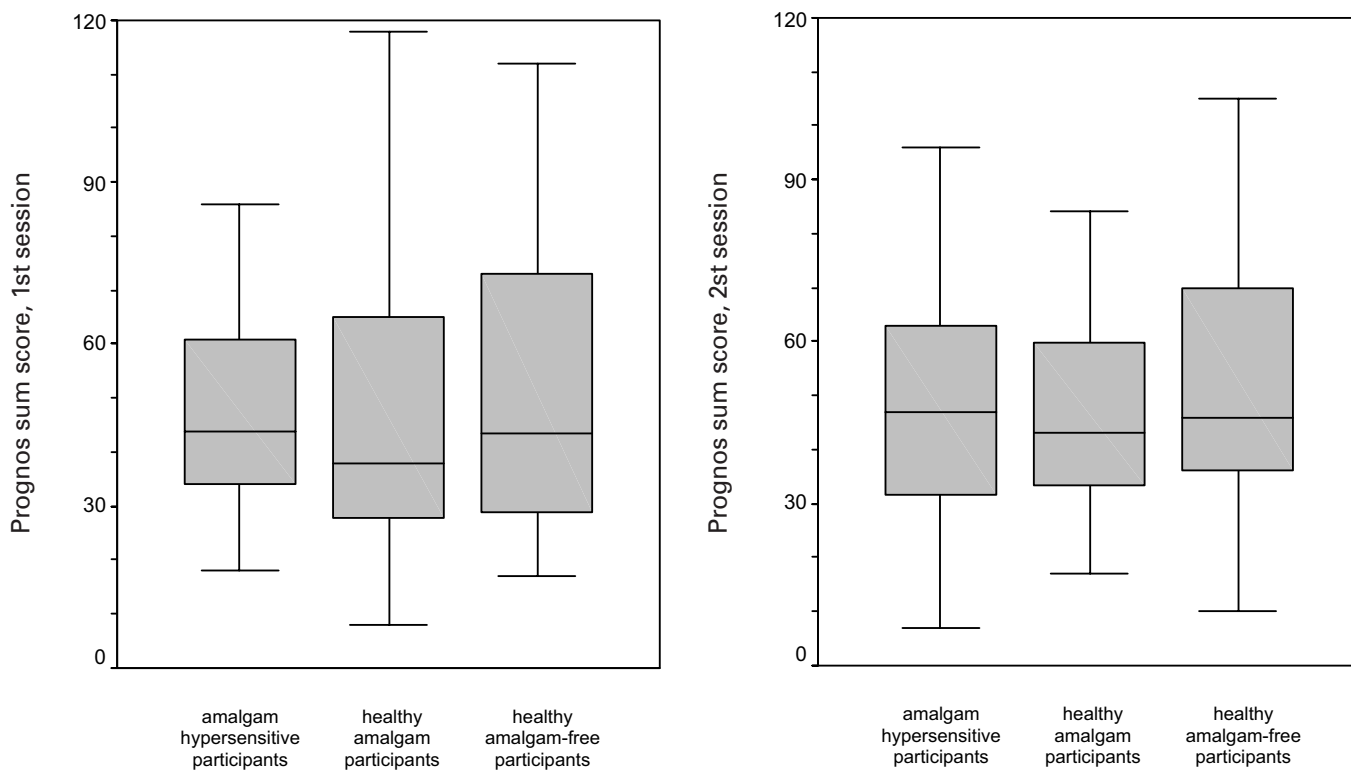


Fig. 2. Comparison of Prognos<sup>®</sup> sum scores in the first and the second session. ● = Amalgam hypersensitive participants, ▲ healthy amalgam participants, \* healthy amalgam-free participants.

to history and clinical findings) volunteers between 20 and 65 years with  $\geq 5$  amalgam surfaces. Group 3 (healthy amalgam-free individuals, controls II) consisted of 27 healthy volunteers who were free of and never had any amalgam fillings and who did not have any known specific mercury or amalgam exposure. Volunteers with  $> 7$  mild symptoms on the list of 50 symptoms were not included in groups 2 and 3.

Participants for group 1 were recruited out of a pool of applicants for a therapeutic study which was advertised in local newspapers. In this thera-



**Fig. 3.** Prognos<sup>®</sup> sum scores in the 1st and 2nd session in amalgam hypersensitive participants, healthy amalgam participants and healthy amalgam-free participants (median and quartiles).

peutic study, participants were included if they had only amalgam as dental fillings or in combination with composite. Participation in the diagnostic study described here was offered to all other applicants with additional dental fillings like gold, metal or ceramics, if they fulfilled all necessary criteria mentioned above. Healthy control participants were recruited from local universities by advertisements on bulletin boards. All participants received oral and written information on the study and gave informed consent. The study protocol was approved by the ethics committee of the Medical Faculty of the Technische Universität München, Germany.

#### Measurements

All study participants underwent the same set of tests in the same chronological order (fig. 1). On the first visit: Prognos<sup>®</sup> session 1, one blood sampling for a lymphocyte transformation test (LTT), one blood sampling for measuring mercury in plasma and red blood cells, and finally saliva sampling for measuring mercury. 48 h before the second visit all participants had to start a 24-hour collection of urine at home. Then 300 mg Dimaval<sup>®</sup> (Heyl; Berlin, Germany) had to be taken orally and urine was collected for another 24 hours until the morning of the 2nd Prognos<sup>®</sup> testing when all urine samples were returned. All biological samples were blinded and either transferred to the relevant examiner within 10 hours or frozen. Measurements of mercury in blood, urine and saliva were performed in a cold vapor atomic absorption spectrometer. All printouts of Prognos<sup>®</sup> testings were blinded and sent to a Prognos<sup>®</sup> expert.

This manuscript focuses on methods and results for the Prognos<sup>®</sup> testing. Details on the methods and results of the other diagnostic tests used in this study will be published separately.

*Prognos<sup>®</sup> test.* A Prognos<sup>®</sup> instrument and software (V 4.12) were kindly provided by the manufacturer (Medprevent GmbH and Co; Nagel, Ger-

many). Prognos<sup>®</sup> testing is based on the hypothesis of EAV (electroacupuncture according to Voll). The patient is included in a low-current electric circuit and tested with different 'offending' substances. It is assumed that these substances have typical electromagnetic frequencies that produce measurable variations of the cutaneous electric potential. Changes are measured at the terminal points of the meridians where the electrical conductance is particularly high.

According to the manufacturer of Prognos<sup>®</sup> a clear correlation exists between the skin resistance and the energy supply; the higher the resistance value (k $\Omega$ , kilohm) the less favorable is the energetic supply of the meridian and vice versa [9]. Because of these principles Prognos<sup>®</sup> is used both as a diagnostic device and to verify a therapy.

In our study all participants were tested twice for amalgam hypersensitivity in a standardized procedure on separate days. The testing was performed by a researcher (WK) who had been trained by an expert of this method until training and performance were considered adequate. The same expert analyzed the measurements.

From all participants the resistances in k $\Omega$  were measured at the starting and end points (finger and toe nails) of the 12 meridians. After a first 'main' measurement, a stimulation of acupuncture point LG20 with a device called bio comb was performed and a second 'stimulated' measurement was recorded. To identify a possible amalgam hypersensitivity, a special set of 6 substances (stored in small glass vessels) recommended by the manufacturer of Prognos<sup>®</sup> was then used for comparative measurements: Amalgam D10, Amalgam D200, Amalgam pure (same preparation as used in dental practice), Chlorella, Coriander and Toxinex (liquid preparation of Derivatio H). These substances were held in one hand by the participant while the examiner measured all meridian points on the opposite side. Then glass vessel and measurements swapped sides and the remaining meridian points were measured. The software of the Prognos<sup>®</sup>

**Table 1.** Characteristics of participants: values are absolute numbers (percentages) or medians (ranges)

	Amalgam hypersensitive participants (n = 27)	Healthy amalgam participants (n = 27)	Healthy amalgam-free participants (n = 27)
Female	14 (52%)	16 (59%)	22 (82%)
Age (years)	40 (25–60)	28 (21–55)	23 (20–29)
Amalgam fillings	7 (3–17)	7 (3–16)	–
Amalgam surfaces	14 (5–33)	12 (5–37)	–
Symptom score	43 (28–78)	3 (0–7)	4 (0–7)
Number of symptoms at least mild	30 (20–37)	3 (0–7)	4 (0–7)
Number of symptoms at least moderate	10 (7–25)	–	–
Years since first amalgam filling	27 (13–40)	15 (2–35)	–

**Table 2.** Diagnostic test results: values are means (sd), p-values from Kruskal-Wallis test

	Amalgam hypersensitive participants	Healthy amalgam participants	Healthy amalgam-free participants	p-value
<i>Prognos<sup>®</sup> first session (n = 76)</i>				
Sum score	47.83 (18.60)	49.38 (25.94)	52.04 (41.26)	0.83
Amalgam D10	–6.96 (11.42)	–5.73 (18.33)	1.92 (12.33)	0.08
Amalgam D200	–2.96 (16.32)	–4.96 (16.92)	–8.65 (30.34)	0.89
Pure amalgam	–3.08 (16.78)	0.73 (11.96)	–2.31 (13.14)	0.58
Chlorella	–0.21 (9.72)	–1.50 (15.49)	0.81 (12.67)	0.90
Toxinex	1.04 (13.31)	–4.04 (14.97)	–5.04 (16.33)	0.60
Coriander	–6.17 (15.15)	–1.35 (13.74)	3.46 (17.65)	0.09
<i>Prognos<sup>®</sup> second session (n = 73)</i>				
Sum score	55.35 (33.74)	57.32 (33.23)	50.00 (30.18)	0.70
Amalgam D10	–6.00 (21.60)	–11.92 (25.38)	–5.58 (21.87)	0.59
Amalgam D200	–2.95 (15.87)	–0.16 (10.86)	0.88 (12.19)	0.76
Pure amalgam	0.55 (13.06)	–5.56 (15.19)	–6.15 (13.80)	0.05
Chlorella	–0.84 (14.05)	–1.92 (17.28)	1.23 (17.91)	0.96
Toxinex	–3.32 (13.94)	3.56 (16.11)	–0.73 (14.05)	0.53
Coriander	3.09 (12.83)	–3.36 (15.65)	–4.27 (15.94)	0.29

device set the first main measurement to zero as a bench mark for further measurements. The following measurements were given as deviations in percentage from this bench mark. The findings of the 6 substance tests were combined in a sum score which was postulated to be sensitive for amalgam hypersensitivity. Based on this sum score and the pattern of results the Prognos<sup>®</sup> expert made a dichotomized diagnostic conclusion.

**Lymphocyte transformation test (LTT).** 20 ml of venous blood were taken with a syringe pretreated with heparin, and another 10 ml of venous blood in a syringe not pretreated. The laboratory which performed the LTT in our study used a variation of the common LTT [10] in order to increase sensitivity. To identify possible amalgam hypersensitivity a set of metals was tested including inorganic mercury, methyl-, ethyl- and phenyl-mercury, amalgam, copper, silver and tin. Out of this list amalgam and inorganic mercury were predefined as the most specific test substances.

**Mercury in blood.** 10 ml of venous blood were taken with a syringe (pretreated with EDTA). Plasma and red cells were separated by centrifugation. Mercury was determined in each fraction by cold vapor atomic absorption spectrometry. Inorganic and total mercury were measured in duplicates and the amount of organic mercury was determined by the subtraction of inorganic mercury means from total mercury means [11].

**Mercury in urine and mercury mobilization.** Between the first and the second Prognos<sup>®</sup> testing, all participants had to collect urine for 24 hours before and for 24 hours after taking 300 mg tablets of Dimaval<sup>®</sup> orally at home [12, 13]. Collection was done in 2.5 l polyethylene bottles containing 2 ml of 10% nitric acid to prevent reduction and volatilization of mercury.

Urine samples were handed in immediately after the second collection when the participant returned for the second Prognos<sup>®</sup> testing.

**Saliva testing (chewing gum test).** Simultaneous to the blood sampling a chewing gum test was performed at the first interview [14]. All participants gave a spontaneous saliva sample of 5 ml (non activated saliva) and another 5 ml after extensive use of a chewing gum (activated saliva). To avoid excessive results special attention was given to thorough centrifugation in order to separate small particles of amalgam that may have been collected accidentally in the sample.

#### Statistics

All data analysis was performed with SPSS<sup>®</sup> (Version 11.5, SPSS Inc., Chicago, IL, USA). Main outcome measures for the two parts (agreement of findings obtained at two separate sessions; correlation testing) of the study were defined beforehand. Main outcome measure of the first part was agreement above chance (quantified by Cohen's Kappa) for the dichotomized (amalgam burden yes/no) Prognos<sup>®</sup> test results of the two diagnostic sessions in each participant. As secondary outcomes we calculated Spearman correlation coefficients and intraclass correlation coefficients (ICC; 2-way mixed models) for the summary score and the 6 single substance tests. Main outcome measure for the second part was the correlation between the Prognos<sup>®</sup> sum score at the first session and a combination score for mercury in saliva after chewing gum and 24-hour urine after mobilization with Dimaval<sup>®</sup>. This score was chosen on recommendation of the Prognos<sup>®</sup> expert and calculated as follows: Findings from urine and

**Table 3.** Diagnostic test results: values are means (sd), p-values from Kruskal-Wallis test (Hg = mercury)

	Amalgam hypersensitive participants	Healthy amalgam participants	Healthy amalgam-free participants	p-value
Total Hg in saliva <i>before</i> chewing gum (ng/ml)	1.10 (1.70)	1.28 (1.67)	0.04 (0.03)	<0.001
Total Hg in saliva <i>after</i> chewing gum (ng/ml)	1.04 (0.78)	1.38 (1.79)	0.02 (0.04)	<0.001
Total Hg in saliva <i>before</i> chewing gum (ng)	3.92 (6.83)	5.07 (7.27)	0.16 (0.16)	<0.001
Total Hg in saliva <i>after</i> chewing gum (ng)	3.58 (3.19)	5.31 (7.26)	0.08 (0.16)	<0.001
Inorganic Hg in erythrocytes (ng/ml)	0.43 (0.36)	0.43 (0.35)	0.10 (0.05)	<0.001
Inorganic Hg in plasma (ng/ml)	0.49 (0.44)	0.44 (0.34)	0.08 (0.05)	<0.001
Total Hg in urine <i>before</i> Dimaval® (ng/ml)	0.65 (0.68)	0.77 (0.70)	0.19 (0.14)	<0.001
Total Hg in urine <i>after</i> Dimaval® (ng/ml)	4.26 (5.35)	5.71 (5.45)	0.89 (0.92)	<0.001
Total Hg in urine <i>before</i> Dimaval® (µg/24h)	0.98 (0.92)	1.19 (1.03)	0.26 (0.19)	<0.001
Total Hg in urine <i>after</i> Dimaval® (µg /24h)	7.77 (10.20)	12.69 (18.60)	1.43 (1.45)	<0.001
Combination score total mercury in urine after DMPS + total Hg in saliva <i>after</i> chewing gum	11.12 (4.09)	12.37 (3.70)	3.44 (2.03)	<0.001
LTT inorganic Hg (stimulation index)	3.20 (4.26)	3.23 (3.31)	3.18 (3.96)	0.48
LTT amalgam (stimulation index)	1.94 (1.28)	2.12 (1.87)	1.74 (0.68)	0.86

saliva tests were ranked and divided in 10 groups of equal size. The 10% participants with the highest values were allocated a score of 9, the next 10% a score of 8, and so on. The findings from the two tests were then added resulting in the final score (range 0–18). We also calculated Spearman correlation coefficients for the single Prognos® measurements and findings from blood, urine and saliva. Furthermore we tested whether diagnostic findings differed significantly between the groups both for the summary score and for the 6 single substance tests (Kruskal-Wallis test and Mann-Whitney U test). Finally correlation coefficients for diagnostic findings in the different tests were calculated.

## Results

Table 1 summarizes the characteristics of the participants. Cases tended to be older and less often females than controls. Symptoms of patients were mostly unspecific. The four most frequent symptoms regarding severity and quantity were: general weakness, fatigue, proneness to infections and proneness to stress.

A dichotomized diagnostic statement for both Prognos® tests was available for 72 participants (22 cases, 25 healthy amalgam bearer, and 25 amalgam-free volunteers). There was no agreement above chance between the dichotomized findings (amalgam burden yes/no) in the first and the second Prognos® test (Cohen's Kappa = -0.11, p = 0.30). Of the 33 participants classified as amalgam burdened at the first test, 14 (42%) were classified as not amalgam burdened at the second, and of the 39 tested not amalgam burdened at the first test 27 (69%) were classified amalgam burdened at the second. Comparing the Prognos® sum scores of the two diagnostic sessions against each other provided a similar result (intraclass correlation coefficient = -0.01, 95% confidence interval -0.24 to 0.22; p = 0.53; fig. 2). Agreement for the 6 single substance tests was poor with intraclass correlation coefficients of 0.05 (95% confidence interval -0.19 to 0.28) for Amalgam D10; of 0.08 (-0.15 to 0.31) for Amalgam D200; of -0.05 (-0.28 to 0.18) for

Amalgam pure; of 0.04 (-0.19 to 0.27) for Chlorella; of -0.08 (-0.31 to 0.15) for Coriander; and of -0.22 (-0.43 to 0.01) for Toxinex.

Prognos® sum scores and findings for single substance tests did not differ significantly between cases and controls (fig. 3; table 2). In contrast, significant differences between the three groups were found for urine measurements before and after Dimaval® (mercury in total), blood measurements (inorganic mercury, particularly in plasma), and saliva (table 3). Pairwise comparisons revealed that significant differences were always due to lower mercury or amalgam burden in amalgam-free healthy volunteers while the results in healthy amalgam bearers and cases were similar. The LTT was not able to discriminate between the three groups. There was no correlation between the Prognos® sum score of the first session and the combination score of mercury mobilization after Dimaval® and mercury in saliva after chewing gum (Spearman correlation coefficient = 0.14; p = 0.22). Correlations between the single Prognos® substance tests were low (<0.3) to moderate (maximum value 0.43), correlations with measurements in blood, urine and saliva low (<0.3; table 4).

## Discussion

The main findings of the study can be summarized as follows: (1) There was no agreement above chance between the findings of two diagnostic sessions with the Prognos® device; (2) Prognos® sum scores did not differ in a significant manner between groups, while amalgam-free healthy volunteers had significantly lower mercury levels in blood, urine and saliva; (3) there were no significant differences between patients with suspected amalgam hypersensitivity and healthy amalgam bearers in any test; (4) there was no correlations between Prognos® findings and other diagnostic tests.

**Table 4.** Spearman correlation coefficients ( $r$ ) between measurements with Prognos, in blood, urine and saliva (first measurement session); (Hg = mercury)

	Prognos				Blood			Urine			Saliva		
	Amalgam D200	Amalgam pure	Chlorella	Coriander	Toxinex	Sum score	Inorg. Hg erythrocytes	Total Hg plasma	Inorg. Hg before	Total Hg before DMPS (conc.)	Total Hg before DMPS (amount)	Total Hg before chewing (conc.)	Total Hg before chewing (amount)
Amalgam D10	-0.04	0.06	0.18	0.15	-0.31	-0.01	-0.22	-0.25*	-0.18	-0.21	-0.15	-0.18	-0.18
Amalgam D200		0.07	-0.10	-0.29*	0.25*	-0.62*	-0.01	-0.06	-0.04	0.01	-0.08	-0.10	-0.10
Amalgam pure			-0.28*	-0.09	0.03	-0.21	0.07	0.03	0.04	0.19	0.02	0.04	0.04
Chlorella				-0.04	-0.25*	0.23*	-0.25*	-0.14	-0.16	-0.20	-0.09	-0.09	-0.09
Coriander					-0.43*	0.34*	0.05	0.03	0.05	-0.05	0.02	0.02	0.02
Toxinex						-0.26*	0.17	0.08	0.10	0.14	0.00	0.03	0.03
Sum score							0.17	0.19	0.15	-0.01	0.00	0.02	0.02
Inorg. Hg erythrocytes								0.90*	0.93*	0.64*	0.46*	0.45*	0.45*
Total Hg plasma									0.96*	0.61*	0.65*	0.63*	0.63*
Inorg. Hg plasma										0.74*	0.61*	0.58*	0.58*
Total Hg before DMPS (conc.)											0.84*	0.41*	0.40*
Total Hg bef. DMPS (amount)												0.44*	0.40*
Total Hg bef. chewing (conc.)													0.98*

\*Correlations are statistically significant ( $p < 0.05$ ). Frames indicate correlations of measurements using the same methodology.

### Strengths and Limitations

Strengths of our study include a design with both healthy amalgam bearers and amalgam-free subjects as controls, strict blinding of diagnostic assessments, and inclusion of a variety of methods used for identification of amalgam burden or amalgam hypersensitivity. Most of these methods were directly compared for the first time.

When interpreting the findings of our study some limitations have to be taken into account: (1) We cannot rule out that the mobilization of mercury between the first and the second Prognos<sup>®</sup> test interfered with the Prognos<sup>®</sup> measurements. However, it is very unlikely that the lack of agreement between first and second Prognos<sup>®</sup> tests can only be attributed to the influence of the small diagnostic dose of 300 mg of Dimaval<sup>®</sup>. (2) The researcher who did the Prognos<sup>®</sup> testing (WK) was a novice. On the other hand, he was trained by the expert evaluating the findings until his training and performance were considered adequate. (3) The decision to choose a summarized score of all tested Prognos<sup>®</sup> substances as a main outcome measure was not founded on empirical evidence but on the Prognos<sup>®</sup> expert's assumption that this score might be particularly sensitive. Based on our results it might be justified to examine only the scores for Amalgam D10 and Amalgam pure as main outcome measures in future studies. According to the Prognos<sup>®</sup> expert regarding Amalgam D10 a possible explanation might be that it contains amalgam in a concentration similar to the average rate released by amalgam fillings whereas amalgam pure represents an acute intoxication. However, agreement for measurements obtained at the two separate sessions was poor not only for the summary score but also for all single substance tests including those for Amalgam D10 and Amalgam pure. (4) A major problem is, of course, that it is unclear whether all subjects classified as cases are true amalgam sensitives. As there is no gold standard diagnostic test for this problem and controversy whether this condition exists at all, our study is not a direct validity test. However, it seems plausible to expect that a valid diagnostic tool should at least separate amalgam-free subjects from amalgam bearers. (5) Our cases and controls differed in a variety of aspects such as age or sex. However, such differences would be expected to cause, if anything, an overestimation of the agreement.

### Interpretation

A variety of unconventional diagnostic methods are used to test for amalgam hypersensitivity like bioresonance and kinesi-ology. Although other methods might be applied more frequently, we chose to use Prognos<sup>®</sup> in our evaluation as (1) there is evidence that the measurement of skin resistance with Prognos<sup>®</sup> produces reliable findings [6, 7]; (2) the diagnostic process can be standardized and allows blinded assessments; (3) Prognos<sup>®</sup> experts provided operationalized hypotheses. How can we explain the discrepant findings regarding reliability in previous studies and regarding agreement in our investigation? Treugut et al. [6] and Colbert et al. [7] determined the

reliability of the direct measurements of electrical skin resistance at the meridian points. The measurements taken in these studies correspond to the first 'main' measurement in our study (without stimulation or any substances). Measurements were repeated within a short time period. In our study there were several days up to weeks between the two measurement sessions. Instead of 'raw' skin resistance measurements we used 'integrated diagnostic' values synthesized by the Prognos<sup>®</sup> computer software from measurements at all relevant meridian points with substance testing and compared them with the first 'main' measurement. On which level reliability is actually lost remains unclear.

We are not aware of other empirical investigations of the reliability and validity of Prognos<sup>®</sup> beyond skin-resistance measurement in the peer-reviewed literature. In an unpublished open study the Prognos<sup>®</sup> expert of our team found good agreement of Prognos<sup>®</sup> findings with conventional thyroid function tests. Rigorous studies are clearly desirable. Future diagnostic studies to test validity should preferably be performed in conditions for which an established gold standard diagnostic test exists. Reliability must be tested both at the level of electrical skin measurements and at the level of clinical statements.

The diagnosis of amalgam hypersensitivity is a highly controversial issue. If one or several of the diagnostic tools tested in our study would have reliably discriminated between cases and controls this would have been indirect evidence that amalgam sensitivity is a valid pathological concept. However, the diagnostic methods were only able to detect differences between amalgam-free subjects and amalgam bearers (regardless of their health condition). While our results do not provide support for the concept of amalgam hypersensitivity, it can, of course, not be ruled out, that it is a valid concept.

It is difficult to make recommendations for studies on further diagnostic tools for amalgam hypersensitivity used by practi-

tioners of complementary and alternative medicine. As it is relatively easy to study reliability this should be investigated first. A diagnostic tool which is unreliable is also unlikely to produce valid findings. If a diagnostic tool has been shown, however, to be reliable, we think that indirect validation strategies as used in our study are the only option to proceed.

## Conclusion

In this study Prognos<sup>®</sup> could not be shown to be a useful tool in the diagnosis of disorders suspected to be due to dental amalgam fillings. It is not possible to extrapolate on the reliability and validity of Prognos<sup>®</sup> as diagnostic device for other conditions from our results.

## Acknowledgement

This study is part of the German Amalgam Trial (GAT), funded by the Foundation Association for the Promotion of Sciences and Humanities in Germany (Stifterverband für die Deutsche Wissenschaft).

It is also part of the first author's MD thesis at the Division of Complementary Medicine, Department of Internal Medicine at the Universitätsspital Zürich, Switzerland.

The authors wish to thank every participant of our study. We furthermore thank our medical students and colleagues who contributed to this study. The technical assistance of Bärbel Maier with the mercury analyses is gratefully acknowledged.

In draft versions of this article we had included the Prognos expert for the study, Dr. M. Doepp, as a co-author. As Dr. Doepp could not agree with the remaining authors on a final version of the manuscript he asked us to delete his name from the list of authors.

## Conflict of interest

None.

## References

- 1 Staehle HJ: Gesundheitsrisiken durch zahnärztliche Materialien? Dtsch Arztebl 1994;91:A495–502.
- 2 Hickel R, Meier C, Schiele R, Raab W, Petschelt A: Nebenwirkungen von Amalgam? Eine interdisziplinäre Studie. Dtsch Zahnarzt Z 1991;46:542–544.
- 3 Lindh U, Hudecek R, Danersund A, Erikson S, Lindvall A: Removal of dental amalgam and other metal alloys supported by antioxidant therapy alleviates symptoms and improves quality of life in patients with amalgam-associated ill health. Neuro Endocrinol Lett 2002;23:459–482.
- 4 Langworth S, Björkman L, Elinder CG, Järup L, Savlin P: Multidisciplinary examination of patients with illness attributed to dental fillings. J Oral Rehabil 2002;29:705–713.
- 5 Sagrjanski WA: Akupunktur-Grundlagenforschung im Rahmen der russischen Raumfahrtmedizin. Akupunktur Theorie Prax 1996;24:49–57.
- 6 Treugot H, Görner C, Lüdtke R, Burghardt V: Reliabilität der energetischen Meridianmessung mit Prognos A. Forsch Komplementarmed 1998;5:284–289.
- 7 Colbert AP, Hammerschlag R, Aickin M, McNames J: Reliability of the Prognos Electrodermal device for measurements of electrical skin resistance at acupuncture points. J Altern Complement Med 2004;10:610–616.
- 8 Melchart D, Wühr E, Weidenhammer W, Kremers L: A multicenter survey of amalgam fillings and subjective complaints in non-selected patients in the dental practice. Eur J Oral Sci 1998;106:770–777.
- 9 Medprevent: Diagnosis System, PROGNO<sup>®</sup> V3.11 Manual 1998, Nagel/Germany.
- 10 Stejskal VD, Danersund A, Lindvall A, Hudecek R, Nordman V, Yaqob A, Mayer W, Bieger W, Lindh U: Metal-specific lymphocytes: biomarkers of sensitivity in man. Neuro Endocrinol Lett 1999;20:289–298.
- 11 Roschig M, Wünsch G: Quecksilber; in Schmidt P (ed): Biologische Kontrollmethoden in der Arbeitsmedizin. Berlin, Volk und Gesundheit, 1988, pp 375–397.
- 12 Schiele R, Schaller KH, Weltje D: Mobilisation von Quecksilber-Speicherungen im Organismus mittels DMPS (Dimaval<sup>®</sup>). Arbeitsmed Sozialmed Präventivmed 1989;24:249–51.
- 13 Schuurs A, Exterkate R, ten Cate JM: Biological mercury measurements before and after administration of a chelator (DMPS) and subjective symptoms allegedly due to amalgam. Eur J Oral Sci 2000;108:511–522.
- 14 Leisteuvo J, Leisteuvo T, Helenius H, Pyy L, Österblad M, Huovinen P, Tenovuo J: Dental amalgam fillings and the amount of organic mercury in human saliva. Caries Res 2001;35:163–166.