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# Non-allergy-related dental and orofacial findings in 625 patients reporting on adverse effects from dental materials

Fabian Cieplik<sup>a,\*</sup>, Karl-Anton Hiller<sup>a</sup>, Gottfried Schmalz<sup>a,b</sup>,  
Pauline Mittermüller<sup>a,1</sup>, Wolfgang Buchalla<sup>a,1</sup>

<sup>a</sup> Department of Conservative Dentistry and Periodontology, University Hospital Regensburg, Regensburg, Germany

<sup>b</sup> Department of Periodontology, School of Dental Medicine, University of Bern, Bern, Switzerland

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## ABSTRACT

**Objective.** In a cohort of 500 patients complaining about adverse effects from dental materials, allergies were found to be contributing to the patients' subjective complaints in only about 14% of the cases. Therefore, the aim of this retrospective study was to investigate an enlarged cohort of 625 patients reporting on adverse effects from dental materials on non-allergy-related dental or orofacial findings with relevance for their subjective complaints.

**Methods.** 625 patients visiting a specialized consultation on suspected adverse effects from dental materials were characterized regarding age and sex distribution, subjective complaints, allergies, and dental and orofacial findings with relevance for their subjective complaints.

**Results.** This cohort comprised about 81% females and the median age was 58 years. The most often reported subjective complaints were burning mouth (43.8%), taste disorders (28.8%) and dry mouth (22.7%). Allergies toward dental materials were found in 12.3%. In 28.0% of the patients, no dental or orofacial findings with relevance for the subjective complaints expressed by the patients could be found. 19.8% of the patients exhibited relevant functional symptoms, 16.2% relevant orofacial diseases, 15.2% relevant mechanical irritations, 10.1% or 9.4% relevant tooth-related or plaque-related symptoms, respectively, 9.4% hyposalivation, and in 7.2% relevant manufacturing faults were found.

**Significance.** In patients complaining about adverse effects from dental materials, a wide variety of dental or orofacial findings need to be considered despite allergies, although a quarter of the patients did not present any relevant dental or orofacial finding. Therefore, specialized consultations and close collaboration with experts from other fields are eligible.

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\* Corresponding author at: Department of Conservative Dentistry and Periodontology, University Hospital Regensburg, Franz-Josef-Strauß-Allee 11, 93053 Regensburg, Germany.

E-mail address: [fabian.cieplik@ukr.de](mailto:fabian.cieplik@ukr.de) (F. Cieplik).

<sup>1</sup> These authors share senior authorship.

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## 1. Introduction

Contemporary dentistry uses a wide variety of dental materials for restoring lost dental hard tissues or for replacing teeth. These dental materials are mostly intended to remain in the oral cavity for several years or even decades. As an inevitable consequence, adverse effects have been reported to be caused from these materials [1–8]. However, the prevalence of adverse effects from dental materials is quite low [1–3,9,10]. In a series of studies, Jacobsen and Hensten-Pettersen estimated the frequency of adverse effects from dental materials to be 1:300 in prosthodontic patients [3], 1% in orthodontic patients [1] and about one case per year per periodontologist [2], whereby also adverse effects on mouthwashes or latex gloves were included in these studies. Kallus and Mjör reported on 46 cases of adverse effects out of 13,325 patients (0.35%) [10].

Based on a previous study on patients complaining about adverse effects from dental alloys (except amalgams) conducted from 1995 till 1997 [7], a specialized consultation was installed in the Department of Conservative Dentistry and Periodontology of the University Hospital Regensburg in 1998 for patients complaining about suspected adverse effects from dental materials [8]. Until mid of 2019, 625 patients were examined and diagnosed by one single experienced general dentist (Pauline Mittermüller, née Garhammer). Recently, data on frequencies, subjective complaints, objective intraoral symptoms and allergies from the first 500 patients (examined and diagnosed till beginning of 2015) out of this patient cohort was published [8]. In that study, allergies towards dental materials or components of them were found to be contributing to the subjective complaints expressed by the patients in only 14% of the cases [8]. This raises the question which other factors may be causative for the claimed adverse effects from dental materials in this group of patients. Therefore, the aim of the present study was to investigate an enlarged cohort of 625 patients reporting on adverse effects from dental materials (examined and diagnosed between end of 1998 and mid of 2019) retrospectively on non-allergy-related dental or orofacial findings with relevance for their subjective complaints.

## 2. Material and methods

### 2.1. Study design

This retrospective study included data from all patients, who visited the specialized consultation for suspected adverse effects from dental materials in the Department of Conservative Dentistry and Periodontology of the University Hospital Regensburg between end of 1998 and mid of 2019. No further inclusion or exclusion criteria were applied. These 625 patients came on their own initiative, or they were referred to the specialized consultation by dentists from the region of Eastern Bavaria (Niederbayern and Oberpfalz) with about two million inhabitants. All data of this study were retrieved retrospectively and processed completely anonymized ensuring that no allocation of data to the identity of an individual patient was possible. Therefore, no ethical approval of an

institutional review board was required for this type of retrospective study.

### 2.2. Medical anamnesis and clinical examinations

Medical history, medications and allergies were asked from the patients in a standardized manner. First, general (general health) and specific (oral health) anamneses were taken, including information on type, location, time of appearance and duration of the subjective complaints expressed by the patients. Allergies were not the main interest of the present study, but are reported for the sake of completeness (for methods please see Ref. [8]). Second, thorough extraoral and intraoral examinations and photo documentations were taken regularly, while X-ray examinations (mainly orthopantomograms and dental films) were performed in case of justifying medical indications only.

Margins of fixed dental prostheses (FDPs) such as partial crowns, crowns or double crowns were evaluated using dental explorers (EXTU17, EXD3CH6 & EXS96; Hu-Friedy, Chicago, IL, USA) and were defined as insufficient margins if they could be probed (dichotomic decisions based on a simplification of the criteria defined by Felton et al. [11]). Briefly, the explorer was placed on the crown and moved apically onto the unprepared tooth and then moved occlusally onto the crown. The tip of the explorer was angled in both marginal or occlusal direction to detect minute discrepancies in marginal adaptation at the tooth-crown interface [11]. Removable dental prostheses (RDPs) were examined for insufficient hold, swaying upon pressure, irritating ridges or pressure bruises. All FDPs and RDPs were also examined visually for manufacturing faults such as corrosion spots, shrink holes, solder points, perforations, insufficient gold coatings, defective veneering, insufficient relining, irritating splintings etc. Manufacturing faults or mechanical irritations were defined as relevant if they were in close spatial and temporal connection to the subjective complaints expressed by the patients and could be considered causative for these subjective complaints according to profound clinical expertise of the examiner.

Clinical functional analyses were carried out according to the condensed temporomandibular disorders screening based on Krogh-Poulsen [12,13]. This included clinical examination and interview of the patients with regard to oral parafunctional habits (like tongue pressing, cheek chewing, mouth breathing or visceral swallowing patterns), bruxism, pressing and grinding of teeth, abraded dentition, pain on palpation of the masticatory muscles, clicking or pain in the temporomandibular joint, bite discrepancies (e.g. Angle class II or III bite, progenia, crossbite), unclear dental occlusion (e.g. non-occlusion, infra-occlusion), loss of vertical dimension of occlusion, muscular tension or pain in the neck and back, and occlusal interferences of the dental prostheses (e.g. early contacts). Clinical functional diagnoses were deemed relevant if they were in spatial and temporal connection to the subjective complaints expressed by the patients and could be considered causative for these subjective complaints according to profound clinical expertise of the examiner.

The gingiva, oral mucosa and tongue were visually investigated for changes or pathologies related to orofacial diseases (e.g. leukoplakia, oral lichen planus, anomalies of the tongue).

For discerning orofacial diseases from plaque-related symptoms such as gingivitis or denture stomatitis, professional tooth cleaning was performed and patients were asked to rinse with 0.2% chlorhexidine digluconate containing mouthrinse for at least one week prior to re-examination. Orofacial diseases were defined as relevant if they were in close spatial and temporal connection to the subjective complaints expressed by the patients and could be considered causative for these subjective complaints according to profound clinical expertise of the examiner.

The flow rate of stimulated saliva was measured by letting the patients collect gum-stimulated whole saliva during a period of 5 min. Stimulated salivary flow of  $\leq 0.7$  mL/min was considered as hyposalivation [14]. The level of oral hygiene was assessed by means of the full-mouth Papilla Bleeding Index (PBI) as described by Saxer and Mühlemann [15]. All clinical examinations were performed by one experienced dentist with more than 20 years of clinical experience in examining and diagnosing patients with suspected adverse effects from dental materials (PM).

### 2.3. Data analysis

Full-mouth PBI data are given as medians including 1<sup>st</sup> and 3<sup>rd</sup> quartiles. All other data are presented descriptively as frequency tables.  $\chi^2$  tests were applied for comparing all patients and patients with most frequent subjective complaints (i.e. burning mouth, taste disorders, dry mouth) for each relevant dental or orofacial diagnosis obtained. All calculations and statistical analyses were performed using SPSS, v. 25 (SPSS Inc., Chicago, IL, USA).

## 3. Results

### 3.1. Patient characteristics

From the 625 patients in this study, there were 505 females (80.8%) and 120 males (19.2%). The median (1<sup>st</sup>; 3<sup>rd</sup> quartile) age of all patients was 58 (50; 66) years. Full-mouth PBI could be examined in 579 (92.6%) out of the 625 patients. In the remaining 46 patients, PBI could not be measured because these patients were either edentulous, refused measurements or suffered from diseases (e.g. valvular transplants) that argued against PBI measurements without preventive systemic antibiotics. The median (1<sup>st</sup>; 3<sup>rd</sup> quartile) full-mouth PBI was found to be 40.0% (29.6%; 52.5%) in the available 579 patients.

### 3.2. Subjective complaints

Table 1 reports the most frequent subjective complaints expressed by the patients. 2.1% of the patients did not report on any subjective complaint, e.g. due to abatement of the complaints before their appointment in our specialized consultation. The most often reported subjective complaints were burning mouth (43.8%), taste disorders (i.e. metal, sour, bitter, salty, sweet or reduced taste; 28.8%), dry mouth (22.7%), toothache/jaw pain (20.3%), gingivitis (17.1%), and paresthesia (14.1%). The list of subjective complaints expressed by less

**Table 1 – Subjective complaints reported by the 625 patients.**

| Subjective complaint <sup>a</sup>                                    | Frequency (%) <sup>b</sup> |
|--|----------------------------|
| No subjective complaint  | 2.1                        |
| Burning mouth  | 43.8                       |
| Taste irritations (metal, sour, bitter, salty, sweet, reduced taste) | 28.8                       |
| Dry mouth  | 22.7                       |
| Toothache/jaw pain   | 20.3                       |
| Gingivitis   | 17.1                       |
| Paresthesia  | 14.1                       |
| Weakness   | 8.8                        |
| Gingival bleeding  | 7.2                        |
| Headache/migraine  | 6.6                        |
| Swelling   | 6.1                        |
| Intestinal problems  | 5.6                        |
| Sensation of pressure  | 5.4                        |
| Electrical sensations  | 5.3                        |
| Painful swallowing/sore throat                                       | 5.1                        |
| Reduced sense of taste   | 5.1                        |
| Gingival pain  | 4.8                        |
| Red palate   | 4.8                        |
| Articular pain   | 4.2                        |
| Poor denture retention   | 4.0                        |
| Itching  | 3.7                        |
| Red/inflamed tongue  | 3.7                        |
| Dry lips   | 3.5                        |
| Facial pain  | 3.4                        |
| Blisters   | 3.2                        |
| Reduced ability for chewing  | 3.2                        |

<sup>a</sup> Subjective complaints reported by at least 3% of the 625 patients are listed.

<sup>b</sup> 100% = 625 patients, multiple entries per patient were possible. 83 patients (13.3%) reported one subjective complaint, 154 (24.6%) two, 125 (20.0%) three, 110 (17.6%) four and 140 patients (22.4%) reported five or more (up to 12) subjective complaints.

than 3% of the patients comprised 117 entries, e.g. speech impairment, problems with the eyes, sleep disorders, alopecia, nervousness, anxiety states or forgetfulness. 83 patients (13.3%) reported one subjective complaint, 154 (24.6%) two, 125 (20.0%) three, 110 (17.6%) four and 140 patients (22.4%) reported five or more (up to 12) subjective complaints.

### 3.3. Relevant dental and orofacial findings

Table 2 summarizes dental and orofacial findings that were considered relevant for the subjective complaints expressed by the patients. In 175 patients (28.0%), no relevant dental or orofacial findings could be diagnosed. One relevant dental or orofacial finding was diagnosed in 307 patients (48.8%), while two were found in 115 patients (18.7%), three in 26 patients (4.2%) and four in two patients (0.3%).

The most frequently found dental or orofacial findings with clinical relevance for the subjective complaints expressed by the 625 patients were functional symptoms (diagnosed in 19.8% of the patients), orofacial diseases (16.2%) and mechanical irritations caused by FDPs or RDPs (15.2%). Allergies were found in 12.3% of the patients. Tooth-related and plaque-related symptoms accounted for 10.1% or 9.4%, respectively, while hyposalivation was diagnosed in 9.4% of the patients.

**Table 2 – Dental or orofacial findings from the 625 patients with clinical relevance for their subjective complaints.**

| Relevant dental or orofacial finding <sup>1</sup>                               | Frequency (%) <sup>2</sup> |                            |                              |                        |
|---|----------------------------|----------------------------|------------------------------|------------------------|
|   | All <sup>a</sup>           | Burning mouth <sup>b</sup> | Taste disorders <sup>c</sup> | Dry mouth <sup>d</sup> |
| No relevant dental or orofacial finding   | 28.0                       | 26.6                       | 24.4                         | 22.5                   |
| Functional symptoms <sup>3</sup>  | 19.8                       | 26.6***                    | 25.0*                        | 26.1*                  |
| Orofacial diseases <sup>4</sup>   | 16.2                       | 17.5                       | 11.1*                        | 15.5                   |
| Mechanical irritations caused by FDPs or RDPs <sup>5</sup>                      | 15.2                       | 16.8                       | 12.2                         | 14.8                   |
| Allergies   | 12.3                       | 8.8*                       | 12.8                         | 7.0*                   |
| Tooth-related symptoms (e.g. dental caries, endodontic or periodontal problems) | 10.1                       | 6.6**                      | 6.7*                         | 7.7                    |
| Plaque-related symptoms (e.g. gingivitis or denture stomatitis)                 | 9.4                        | 7.7                        | 5.6*                         | 9.9                    |
| Hyposalivation  | 9.4                        | 12.8**                     | 10.0                         | 34.5***                |
| Manufacturing faults of FDPs or RDPs <sup>6</sup>                               | 7.2                        | 9.1                        | 15.0***                      | 10.6                   |

<sup>1</sup>All relevant dental or orofacial findings from the 625 patients are listed.

<sup>2</sup>Multiple entries per patient were possible. 175 patients exhibited no relevant dental or orofacial finding (28.0%). 307 patients (49.1%) had one relevant dental or orofacial finding, 115 patients (18.4%) had two, 26 patients (4.2%) three and 2 patients (0.3%) four relevant dental or orofacial findings.

<sup>3-6</sup>Refined evaluations can be found in the matching Tables 3–6, respectively.

Asterisks indicate statistically significant differences between all patients and patients complaining about burning mouth, taste disorders or dry mouth, respectively, for each relevant dental or orofacial diagnosis (\* $p \leq 0.05$ ; \*\* $p \leq 0.01$ ; \*\*\* $p \leq 0.001$ ;  $\chi^2$  tests).

<sup>a</sup> 100% = all 625 patients.

<sup>b</sup> 100% = 274 patients complaining about burning mouth (43.8% of the 625 patients).

<sup>c</sup> 100% = 158 patients complaining about taste disorders (28.8% of the 625 patients).

<sup>d</sup> 100% = 142 patients complaining about dry mouth (22.7% of the 625 patients).

Relevant manufacturing faults of RDPs or FDPs were found in 7.2% of the patients.

Table 2 further summarizes the dental and orofacial findings considered relevant for patients complaining about burning mouth, taste disorders or dry mouth, respectively, which made up the three most frequently obtained subjective complaints (see Table 1). As compared to the whole cohort of 625 patients, those patients complaining about burning mouth exhibited significantly more often relevant functional symptoms and hyposalivation and significantly less often tooth-related symptoms. Patients complaining about taste disorders were significantly more often diagnosed with relevant functional symptoms and manufacturing faults of FDPs or RDPs, while orofacial diseases, tooth-related and plaque-related symptoms were found significantly less often. Patients complaining about dry mouth had significantly less allergies, but significantly more functional symptoms and hyposalivation.

### 3.3.1. Functional symptoms

From 124 patients (19.8% of the 625 patients) diagnosed with relevant functional symptoms, 58 patients (46.8%) had no further relevant dental or orofacial diagnosis, while in 66 (53.2%) at least one further relevant dental or orofacial diagnosis was found (mostly hyposalivation, mechanical irritations caused, and orofacial diseases). Table 3 summarizes all relevant functional symptoms, whereby oral parafunctional habits (like tongue pressing, cheek chewing, mouth breathing or a visceral swallowing pattern; 8.5%), bruxism (7.0%), pain on palpation of the masticatory muscles (5.1%) and clicking or pain in the temporomandibular joint (4.2%) were found most frequently. Fig. 1 shows clinical examples for relevant functional symptoms.

**Table 3 – Functional symptoms diagnosed in the 625 patients with clinical relevance for their subjective complaints.**

| Relevant functional symptom <sup>a</sup>  | Frequency (%) <sup>b</sup> |
|---|----------------------------|
| No relevant functional symptoms   | 80.2                       |
| Oral parafunctional habits (e.g., tongue pressing, cheek chewing, mouth breathing, visceral swallowing pattern) | 8.5                        |
| Bruxism   | 7.0                        |
| Pain on palpation of the masticatory muscles  | 5.1                        |
| Clicking/pain in the temporomandibular joint  | 4.2                        |
| Non-/infra-occlusion  | 2.4                        |
| Pain in the masticatory muscles according to patient's self-report  | 2.2                        |
| Muscular tension in neck and back   | 1.6                        |
| Bite discrepancies (e.g., Angle class III bite, progenia, crossbite)  | 1.4                        |
| Abraded dentition   | 1.1                        |
| Occlusal interferences of dental prosthesis (e.g., early contacts)  | 1.1                        |
| Loss of vertical dimension of occlusion   | 0.5                        |

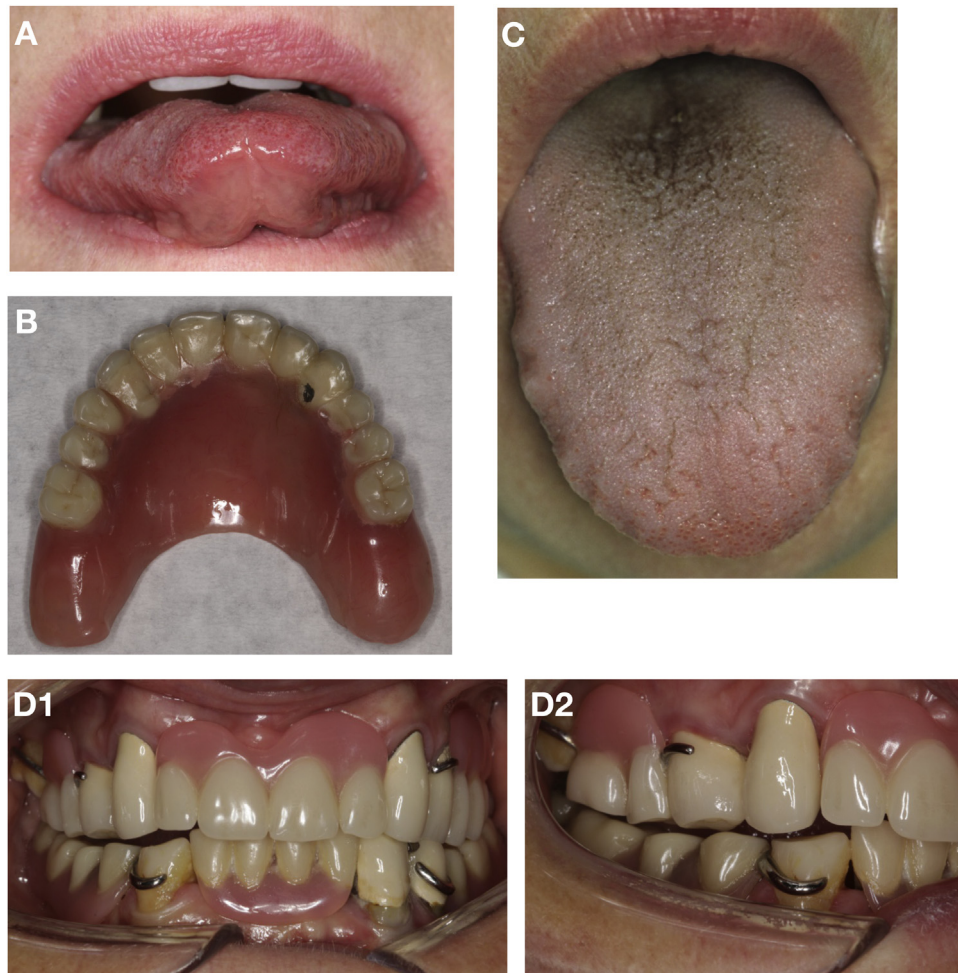
<sup>a</sup> All relevant functional symptoms diagnosed from the 625 patients are listed.

<sup>b</sup> 100% = 625 patients, multiple entries per patient were possible.

### 3.3.2. Orofacial diseases

From 101 patients (16.2% of the 625 patients) diagnosed with relevant orofacial diseases, 57 patients (56.4%) exhibited no further relevant dental or orofacial diagnosis, whereas 54 (43.6%) had at least one further relevant dental or orofacial diagnosis (mostly functional symptoms, hyposalivation and mechanical irritations). Table 4 summarizes all diagnosed oro-





**Fig. 1 – Clinical example for relevant functional symptoms.**

**A: Patient complaining about a burning tip of her tongue due to tongue pressing.**

**B: Upper denture with severe attrition of the denture teeth (particularly in regio 24/25) and multiple chippings of the veneering of the exterior telescopic crown 23 due to severe bruxism in a patient complaining about jaw pain in the maxillary front.**

**C: Patient exhibiting a scalloped tongue due to tongue pressing and a lingua villosa nigra and complaining about burning mouth/tongue.**

**D1, D2: Patient showing non-occlusion on the right side of his RDPs and complaining about burning mouth in the area covered by the RDPs.**

facial diseases, whereby anomalies of the tongue (5.1%) and oral lichen planus (5.1%) were found most frequently. Fig. 2 shows clinical examples for relevant orofacial diseases.

### 3.3.3. Mechanical irritations

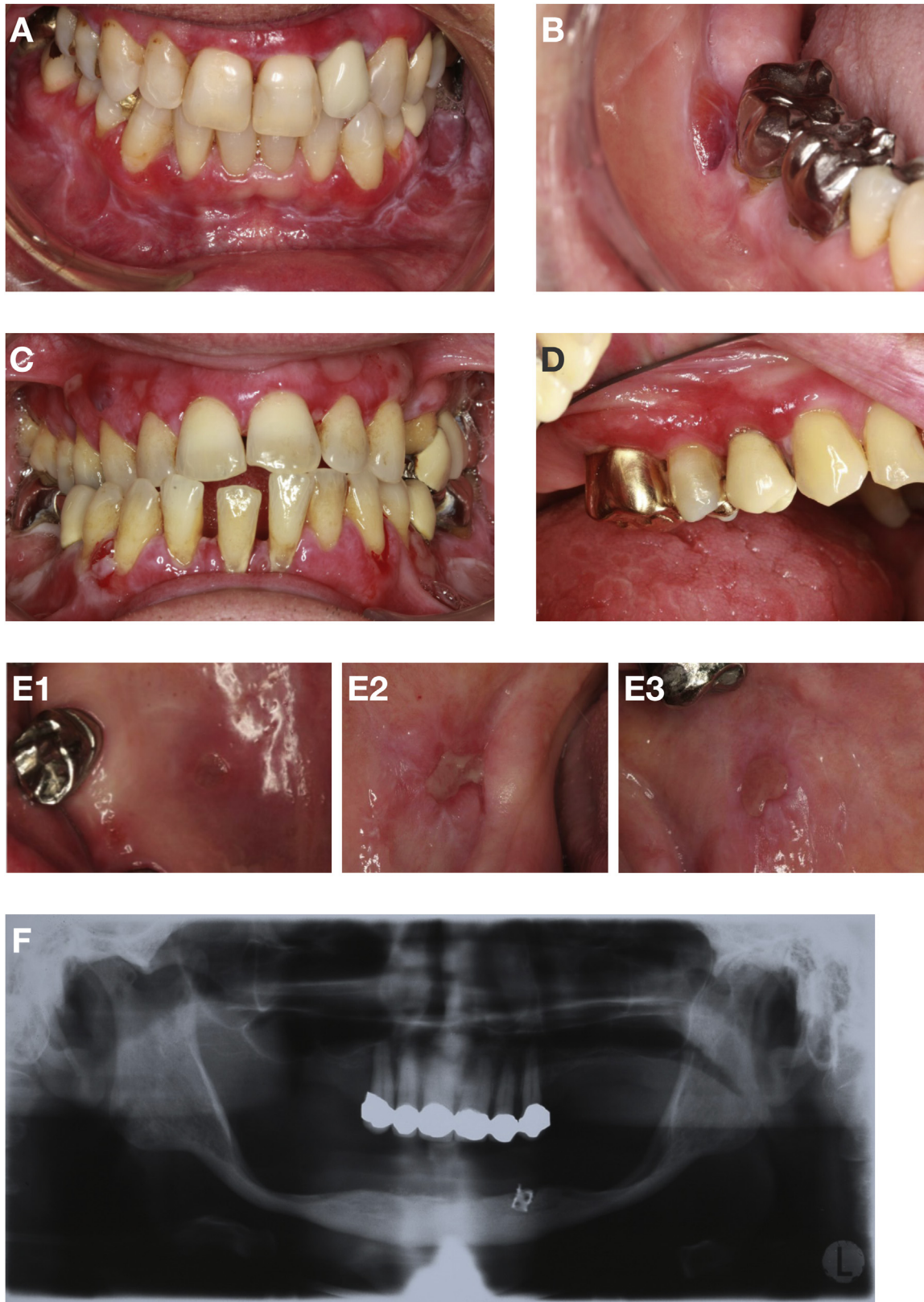
Out of 95 patients (15.2% of the 625 patients) that exhibited relevant mechanical irritations caused by FDPs and RDPs, 28 (29.5%) had no other relevant dental or orofacial diagnosis, while 67 (70.5%) showed at least one other relevant dental or orofacial diagnosis (mostly functional symptoms, plaque-related symptoms and manufacturing faults). Table 5 depicts all relevant mechanical irritations, whereby insufficient margins of FDPs (7.7%), insufficient hold of RDPs (5.0%) or swaying upon pressure of RDPs (4.3%) were found most often. Fig. 3 shows clinical examples for relevant mechanical irritations caused by FDPs and RDPs.

### 3.3.4. Allergies

Seventytwo (93.5%) from 77 patients diagnosed with relevant allergies towards a dental material allergen diagnosed by patch test (12.3% of all patients) exhibited no other relevant dental or orofacial diagnosis. Details on this aspect have been presented earlier [8].

### 3.3.5. Tooth-related symptoms

From 63 patients (10.1% of the 625 patients) diagnosed with relevant tooth-related symptoms such as dental caries, endodontic or periodontal problems, 32 patients (50.8%) had no further relevant dental or orofacial diagnosis, while in 31 (49.2%) at least one further relevant dental or orofacial diagnosis was found (mostly functional symptoms, orofacial diseases and plaque-related symptoms). Fig. 4 shows clinical examples of relevant tooth-related symptoms.



**Fig. 2 – Clinical examples for relevant orofacial diseases.**

**A:** Severe oral lichen planus.

**B:** Bullous pemphigoid.

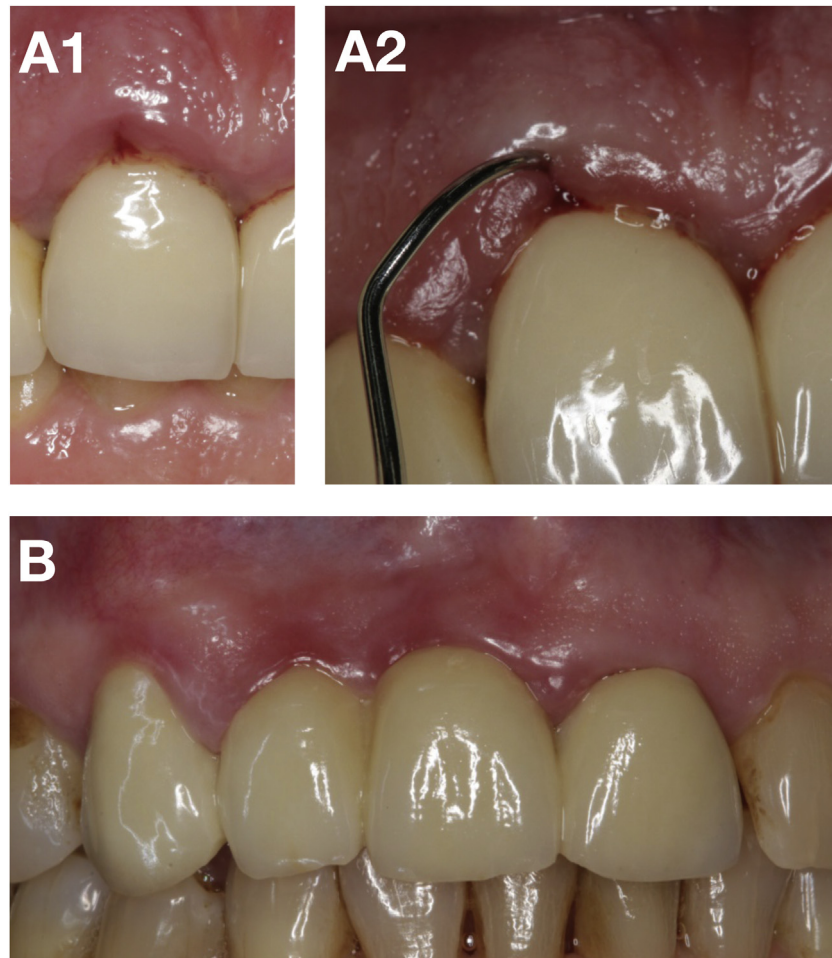
**C:** Pemphigus.

**D:** Erosive oral lichen planus in the upper jaw and combination of lingua plicata and lingua geographica.

**E1, E2, E3:** Three distinct lesions of an oral lupus erythematosus in the same patient.

**F:** Extensive atrophy of the mandibular bone with remnants of an implant in regio 33.

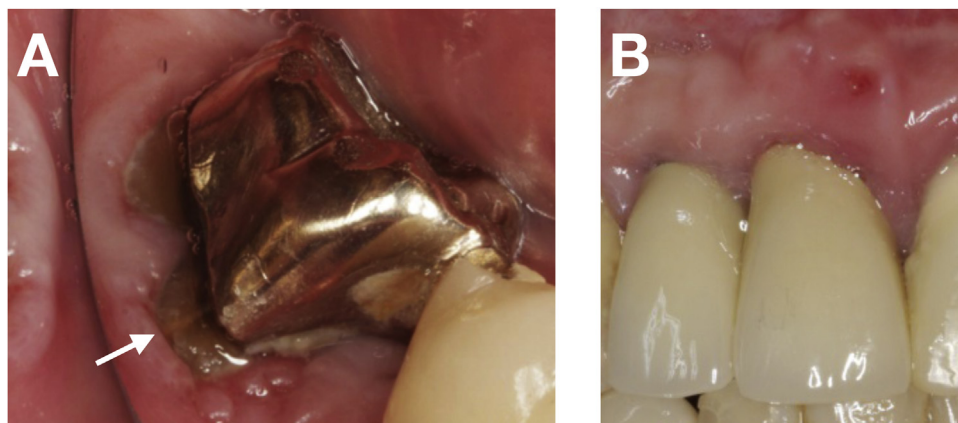




**Fig. 3 – Clinical examples for mechanical irritations.**

**A1, A2: Insufficient margin of an FDP and persisting gingivitis on tooth 11.**

**B: FDP with massive and traumatizing pontics and persisting gingival inflammation in regio 11/12.**



**Fig. 4 – Clinical examples for relevant tooth-related symptoms.**

**A: Toothache and jaw pain due to root fracture on tooth 47.**

**B: Toothache, taste disorders and feeling of pressure in the area of maxillary incisors due to gingival sinus tract and intra-bony periodontal defect at tooth 11.**

**Table 4 – Orofacial diseases diagnosed in the 625 patients with clinical relevance for their subjective complaints.**

| Relevant orofacial disease <sup>a</sup>                              | Frequency (%) <sup>b</sup> |
|--|----------------------------|
| No relevant orofacial disease  | 83.8                       |
| Anomalies of the tongue  | 5.1                        |
| Oral lichen planus   | 5.1                        |
| Generalized lichen planus  | 1.1                        |
| Lichenoid contact reaction   | 1.1                        |
| Fungal infection   | 1.0                        |
| Atrophy of the mandibular bone                                       | 0.8                        |
| Leukoplakia  | 0.8                        |
| Maxillary sinusitis  | 0.6                        |
| Trigeminal neuralgia   | 0.6                        |
| Blistering autoimmune disorders (e.g. pemphigus, bullous pemphigoid) | 0.3                        |
| Atypical facial pain or atypical odontalgia                          | 0.3                        |
| Eagle syndrome   | 0.2                        |
| Gingival hyperplasia   | 0.2                        |
| Oral herpes  | 0.2                        |
| Oral lupus erythematoses   | 0.2                        |
| Sialolithiasis in the parotid gland                                  | 0.2                        |

<sup>a</sup> All relevant orofacial diseases diagnosed from the 625 patients are listed.

<sup>b</sup> 100% = 625 patients, multiple entries per patient were possible.

**Table 5 – Mechanical irritations caused from FDPs or RDPs found in the 625 patients with clinical relevance for their subjective complaints.**

| Relevant mechanical irritation <sup>a</sup> | Frequency (%) <sup>b</sup> |
|---|----------------------------|
| No relevant mechanical irritation           | 84.8                       |
| Insufficient margin (FDP)                   | 7.7                        |
| Insufficient hold (RDP)                     | 5.0                        |
| Swaying upon pressure (RDP)                 | 4.3                        |
| Pressure bruise (RDP)                       | 1.1                        |
| Insufficient ridge (RDP)                    | 0.3                        |
| Irritating splinting (FDP)                  | 0.3                        |

<sup>a</sup> All relevant mechanical irritations found in the 625 patients are listed.

<sup>b</sup> 100% = 625 patients, multiple entries per patient were possible.

### 3.3.6. Plaque-related symptoms

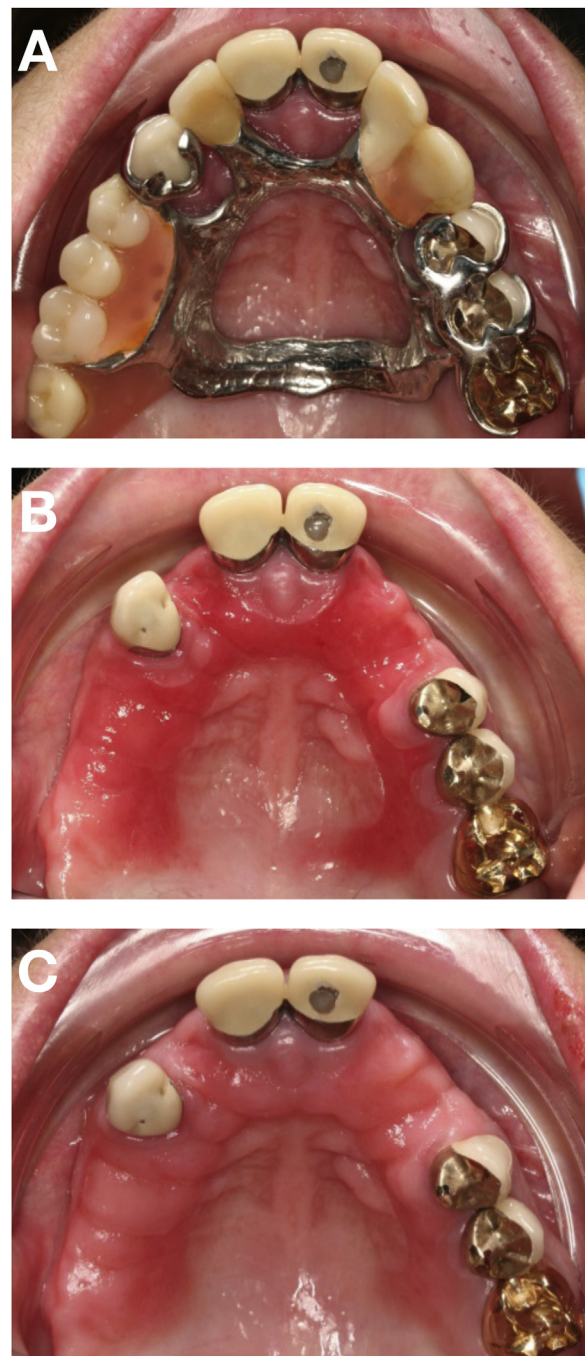
From 59 patients (9.4% of the 625 patients) diagnosed with relevant plaque-related symptoms such as gingivitis or denture stomatitis, 25 patients (42.4%) had no further relevant dental or orofacial diagnosis, while 34 (57.6%) exhibited at least one further relevant dental or orofacial diagnosis (mostly mechanical irritations, functional symptoms and tooth-related symptoms). Fig. 5 shows a clinical example of a relevant plaque-related symptom.

### 3.3.7. Hyposalivation

Out of 59 patients (9.4% of the 625 patients) diagnosed with hyposalivation, 18 patients (30.5%) had no further relevant dental or orofacial diagnosis, while 69.5% had at least one further relevant dental or orofacial diagnosis (mostly functional symptoms, orofacial diseases and mechanical irritations).

### 3.3.8. Manufacturing faults

From 45 patients (7.2% of the 625 patients) diagnosed with relevant manufacturing faults of FDPs or RDPs, 17 patients



**Fig. 5 – Clinical example for a relevant plaque-related symptom: Patient with denture stomatitis manifesting as RDP-congruent redness of the palate (A, B) and after consecutive antibacterial and antifungal therapy with 0.2% chlorhexidine mouthrinse and amphotericin B for one week each (C).**

(37.8%) had no further relevant dental or orofacial diagnosis, while 28 (62.2%) exhibited at least one further relevant dental or orofacial diagnosis (mostly mechanical irritations, hyposalivation and plaque-related symptoms). Table 6 summarizes all relevant manufacturing faults, whereby corrosion spots or shrink holes (3.0%), solder points (2.9%) and perforations (1.4%)



**Table 6 – Manufacturing faults found in FDPs or RDPs of the 625 patients with clinical relevance for their subjective complaints.**

| Relevant manufacturing fault <sup>a</sup> | Frequency (%) <sup>b</sup> |
|---|----------------------------|
| No relevant manufacturing fault           | 92.8                       |
| Corrosion spot/shrink hole                | 3.0                        |
| Solder point                              | 2.9                        |
| Perforation                               | 1.4                        |
| Insufficient gold coating                 | 0.5                        |
| Defective veneering                       | 0.2                        |
| Insufficient relining                     | 0.2                        |

<sup>a</sup> All relevant manufacturing faults found in the 625 patients are listed.

<sup>b</sup> 100% = 625 patients, multiple entries per patient were possible.

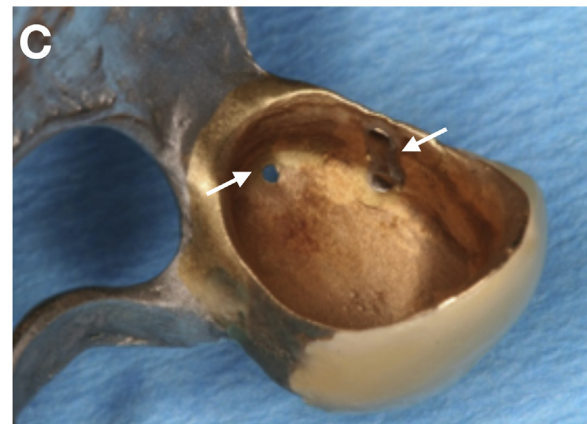
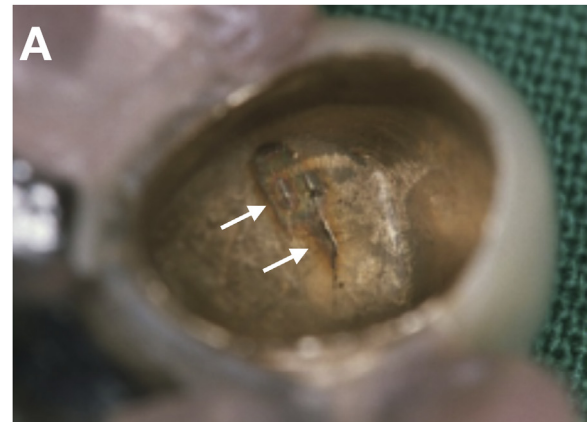
were found most frequently. Fig. 6 shows clinical examples of relevant manufacturing faults.

## 4. Discussion

### 4.1. Study design and study population

In a previous study examining 500 patients reporting on adverse effects from dental materials, we found that allergies towards dental materials or components of them were contributing to these adverse effects in only 14% of the cases [8]. Therefore, the present study focused on non-allergy-related dental or orofacial findings with relevance for the complaints expressed by the patients in an enlarged cohort of 625 patients reporting on adverse effects from dental materials. The design of the present study is based on our previous study [8]. All patients who visited the special consultation for suspected adverse effects from dental materials in the Department of Conservative Dentistry and Periodontology of the University Hospital Regensburg between end of 1998 and mid of 2019 were included into this study without applying any further inclusion or exclusion criteria. During these 21 years, 625 patients with claimed adverse effects from dental materials visited this special consultation, resulting in approximately 30 cases per year. Although these patients came from the well-defined Eastern Bavarian region (Niederbayern and Oberpfalz) with about two million inhabitants, the present study can still not be considered to be an epidemiological study because probably not all general dentists in the area referred patients to the University Hospital Regensburg, and some patients might have refused to visit the specialized consultation despite being referred to.

The exposure to dental materials is known to increase with age due to increasing numbers of restorations and lost teeth that are replaced by dental prostheses [8,16]. This may be one factor that the median age of the patients in this cohort was 58 years, which is in accordance with our previous studies [7,8]. Likewise, Lygre et al. reported 40–59 years to be the most prevalent age group in their study on adverse reactions to dental materials [17], and 58.5 years was found the median age in a case series on burning mouth syndrome [18]. The strong predominance of females (80.8%) in our cohort is in line with other studies [17,19,20]. For instance, Scott et al. also reported four-fold as many women than men reporting on adverse effects



**Fig. 6 – Clinical examples for relevant manufacturing faults.**

**A: Corrosion spot in an exterior telescopic crown.**

**B: Shrink holes on exterior telescopic crowns.**

**C: Exterior telescopic crown with perforation and large solder point.**

from dental materials [19]. Besides some speculations about endocrine changes being accounted for the high proportions of females in middle or elder age groups [21], females may also just be more attentive to their health and consequently more likely to report adverse reactions rather than to generally experience them more often [19,22,23].

The level of oral hygiene of the patients included in this study was assessed by means of the full-mouth PBI, which

was found to be 40.0% in median. Oral hygiene data from other cohorts of patients claiming adverse effects from dental materials are not available so far [8]. The current Fifth German Oral Health Study only investigated age groups that were either slightly younger (younger adults, 35–44 years) or older (younger seniors, 65–74 years) than the cohort described in this study [16]. For these two age groups, mean full-mouth bleeding on probing (BOP) scores of 27.3% or 37.6% were reported, respectively [16]. Since recently a BOP score of 30% or higher was proposed as case definition for generalized gingivitis [24] and a full-mouth PBI score of 40% has also been suggested as a cut-off value to differentiate between excellent to good and fair to poor oral hygiene [25], the cohort investigated in the present study may match the data described in the Fifth German Oral Health Study in terms of oral hygiene and thus may not be characterized by a generally less sufficient oral hygiene level.

#### 4.2. Subjective complaints

The patients described a large range of different subjective local or general complaints which are in line with our previous study [8] and similar to those found in the literature for other cohorts of patients reporting on adverse effects from dental materials [17,20,22,26]. The clinical appraisal of these subjective complaints can be very challenging because patients often report large numbers of different subjective complaints, e.g. up to 12 in the present cohort. These expressed complaints may also not be related to dental materials at all. Even local (i.e. oral) complaints can be caused by systemic diseases or due to side-effects from medications [8]. For instance, burning mouth, which was the most frequently expressed complaint in this cohort, has been linked to numerous etiologies, with current evidence supporting peripheral or central neuropathic changes [18,27]. Taste disorders, which made up the second most often expressed complaint, can be idiopathic, associated with medications or chemicals or have posttraumatic, post-operative or postinfectious etiology [28], and are also strongly associated with burning mouth-related symptoms [29]. Likewise, dry mouth, which was complained about third most often, is on the one hand a potential oral complication of diabetes mellitus [30], but can also be due to smoking, alcohol consumption or often prescribed medications like antidepressants or antihypertensives [31]. Furthermore, dry mouth as a symptom is known to be strongly associated with increasing age [32]. Noteworthy, only 34.5% of the patients complaining about dry mouth in the present cohort also showed objectively measurable hyposalivation, which is in line with the literature [33]. Such subjective perception of dry mouth without objective hyposalivation has been described to be linked to alterations in the visco-elastic properties of the saliva or to changes in the patients' perception mechanisms [33]. Table 2 shows that even the most often reported local complaints burning mouth, taste disorders and dry mouth can be associated to a wide variety of different dental and orofacial findings, while they can additionally be caused by or related to various systemic, psychogenic or medication-related factors. So, a general practitioner still needs to consider the wide variety of potential explanations for a given local complaint rather than to readily choose the most obvious one, when examin-

ing a patient complaining about adverse effects from dental materials.

This situation gets even more complex with general (i.e. non-oral) complaints such as weakness, headache/migraine or intestinal problems, which obviously are not related to the oral cavity and may be caused by various other diseases, but are still allegedly attributed to be adverse effects from dental materials. Tillberg et al. showed that patients expressing systemic or complex (i.e. local and systemic) complaints had an unfavorable prognosis with regard to persistence of their complaints even after replacement of dental restorations as compared to those patients who reported local complaints only [22]. Mårell et al. also reported that patients with complex complaints had a significantly higher level of general psychological distress and somatization than patients with local complaints only [34]. Accordingly, associations between complex complaints and social consequences in daily life have been described [23]. Therefore, dental, medical and social factors must be taken into account simultaneously when examining patients who claim adverse effects from dental materials [8,23].

#### 4.3. Relevant dental and orofacial findings

Allergies relevantly contributed to the complaints expressed by the 625 patients in only 12.3% of the cases, which is in accordance with the findings (14%) from our previous study [8]. Since the role of allergies (including the method of patch testing and the most frequently found allergens) has already been extensively discussed in this previous publication [8], the focus of the present study was set on dental and orofacial findings with potential relevance for the subjective complaints expressed by the patients, which shall be discussed in the following paragraphs.

##### 4.3.1. Functional symptoms

Functional symptoms were recorded using a condensed temporomandibular disorders screening, which however has been discussed critically in recent years due to a potential over-interpretation of the findings [35]. Thus, just oral parafunctional habits and bruxism, which were found most frequently as relevant functional symptoms in the present cohort, shall be discussed here. Habits such as tongue pressing can cause habitual irritations leading to symptoms of burning mouth [27] (see Fig. 1A for a clinical example). Accordingly, patients complaining about burning mouth were significantly more likely to be diagnosed with functional symptoms. This is also in line with the literature, where tongue pressing has been found in about 32% of 101 patients with burning mouth syndrome [36]. Bruxism on the other hand can be associated with myofascial pain and temporomandibular disorders [37], and with tension-type headache and migraine [38]. In general, functional symptoms such as temporomandibular disorders are known to be more common in women [39,40], which may contribute to explain the high prevalence of females in this cohort.

##### 4.3.2. Orofacial diseases

The most frequently found relevant orofacial diseases were tongue anomalies and oral lichen planus. The prevalence of

relevant tongue anomalies in this cohort was found slightly higher (5.1%) than reported by Shulman et al. for a sample of 17,235 US-Americans aged 17 or older (3.11%) [41]. Tongue anomalies like lingua plicata and lingua geographica have been described as anatomical variations related to burning mouth syndrome [42]. Accordingly, we found in a previous study that 10 out of 14 patients with tongue anomalies complained of a burning tongue [7]. Likewise, Picciani et al. reported burning sensations in 45 out of 96 patients with lingua geographica [43]. Oral lichen planus was diagnosed in 5.1% of the 625 patients, while the global prevalence has been reported to be around 1% [44,45]. Since oral lichen planus is more commonly found in middle-aged women [46,47], this may explain the predominance of females in our cohort. Oral lichen planus can be characterized by a wide variety of clinical manifestations [46,47], which often lead to misdiagnosis, particularly in cases where typical mucosal characteristics (so-called Wickham striae) are weakly pronounced or where its symptoms are confined to the gingiva (desquamative gingivitis) [45,47]. Symptomatic oral lichen planus usually presents as burning sensation or pain [46,47], is linked to psychological disorders and can seriously affect oral health-related quality of life [48].

#### 4.3.3. Mechanical irritations

Relevant mechanical irritations can be caused by both FDPs and RDPs. Insufficient margins of FDPs are associated with gingivitis and periodontal bone loss [49,50] and were found in 7.7% of the patients. It is well-known from classic histomorphometric studies that the desired margin quality of FDPs can often not be achieved sufficiently in a clinical setting [49,51]. Regarding RDPs, mechanical irritations can be due to insufficient hold that may also be associated with swaying upon pressure. Mechanical irritations from ill-fitting RDPs can further lead to irritant contact stomatitis (e.g. pressure bruises) [52], and also negatively impact oral health-related quality of life [53]. Poorly fitting RDPs have also been associated with burning mouth-related symptoms [27], but this association was not found significant in the present study.

#### 4.3.4. Tooth-related, plaque-related and hyposalivation-related symptoms

Tooth-related symptoms include dental caries, endodontic or periodontal aspects. Fig. 4A shows a clinical example of a vertical root fracture leading to toothache and jaw pain, which led the respective patient to attend the special consultation. Dental caries and periodontitis are among the most prevalent non-communicable diseases all around the world [54,55], and accordingly 10.1% of the patients in this cohort presented relevant tooth-like symptoms. Plaque-related symptoms comprise gingivitis and denture stomatitis. The prevalence of denture stomatitis has been reported to range from 15% to over 70% among wearers of RDPs with higher prevalence among full denture wearers (particularly in the upper jaw) [56]. Fig. 5 shows a clinical example of denture stomatitis, which could be successfully treated by antibacterial and antifungal agents. Hyposalivation was found in 9.4% of the patients and was significantly associated with dry mouth and burning mouth as subjective complaints. Hyposalivation is known to

be associated with higher incidence of dental caries, gingivitis, oral candidiasis and can also cause burning mouth-related symptoms or taste irritations, thus strongly affecting oral health-related quality of life [57,58]. Hyposalivation is more common in females [58]. Furthermore, it is associated with diagnosed disease and obesity in younger age groups, while it is associated with medication after age 50 [59]. Consequently, the high levels of medication intake and polypharmacy may further increase the prevalence of hyposalivation in an aging society [58].

#### 4.3.5. Manufacturing faults

Manufacturing faults of FDPs or RDPs such as corrosion spots, shrink holes, solder points or perforations were another relevant finding, which could be diagnosed in 7.2% of the patients, but significantly more often in patients complaining about taste disorders. The release of metal ions during corrosion of metal-based FDPs or RDPs has been discussed to be associated with salty or metal taste or burning mouth-related symptoms [60]. Focal pitting corrosion and release of corrosion by-products in nickel-chromium alloys have further been discussed to be responsible for ulcerative lesions of the palate associated with RDPs [61]. Accordingly, metal components from dental materials could be detected in biopsies from adjacent gingival tissues [62] and in saliva [63,64].

## 5. Conclusions

This study shows that – despite allergies – a wide variety of dental or orofacial findings need to be considered in patients complaining about adverse effects from dental materials. Therefore, specialized consultations are eligible that closely collaborate with experts from other dental fields, e.g. periodontologists or maxillofacial surgeons in case of orofacial diseases. Noteworthy, the high prevalence of functional symptoms, hyposalivation and oral lichen planus in this specific cohort may contribute to explain the female predominance in patients claiming adverse effects from dental materials because of the generally higher prevalence of these conditions in women than in men. Still, about one quarter of the patients of this cohort did not present any dental or orofacial finding with relevance to their subjective complaints. Therefore, it is crucial to identify non-orofacial reasons (i.e. systemic, medication-related or psychogenic reasons) for the complaints expressed by the patients.

## Author contributions

All authors conceived and designed the study. PM performed the clinical examinations. KAH, PM, FC, GS and WB analyzed the data. FC wrote the manuscript with input from all authors. All authors reviewed and approved the manuscript.

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