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ORIGINAL ARTICLE

# Evaluation of saliva flow rates, *Candida* colonization and susceptibility of *Candida* strains after head and neck radiation

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**Abstract** Hyposalivation is a long-term effect in patients receiving head and neck radiation. Radiotherapy can predispose oral colonization by *Candida* species of the mucosa. This study aims to evaluate the correlation between hyposalivation, measured by unstimulated saliva flow rates (SFR) and fungal colonization of the oral cavity, and also the resistance of isolated *Candida* strains to antimicrobial therapy. Fifty-three consecutive patients with radiotherapy were examined for late radiation damage on dental hard tissue and the salivary glands (SFR over a period of 5 min). The SFR were divided into three different values of hyposalivation: grade I (SFR 0.1–0.25 ml/min), grade II (SFR ≤0.1 ml/min), and grade III (SFR=0.0 ml/min). Candidal colonization was defined using Sabouraud agar and identified using API 20C AUX (biomerieux) in the patients' rinsing water. Susceptibility was tested with Etest (amphotericin B, ketoconacole, voriconacole, and fluconacole). Hyposalivation grade I was detected in 23% ($9.1\times10^1$ colony forming units (cfu); range, 200–5,900 cfu), hyposalivation grade II in 26% ($4.3\times10^1$ cfu; range, 110–3,300 cfu), and hyposalivation grade III in 51% ($2.0\times10^3$ cfu; range, 300–19,475 cfu) of patients. A significant correlation between the SFR and candidal colonization and clinical presentation (European Organization for Research and Treatment of Cancer (EORTC) score) was detected (Mann–Whitney test, $p=0.031$). Twenty *Candida albicans* and 27 non-*albicans* species were identified. The resistance of *C. albicans* was higher than that of non-*albicans* strains against antimicrobial agents. By comparison, amphotericin B showed the greatest and fluconazole the least effect. A higher value of hyposalivation correlates with a higher risk of candidal colonization in patients who have received radiotherapy and also with a higher EORTC score. The spectrum of *Candida* is wide and susceptibility against antifungal therapy differs. In long-term examinations of patients with xerostomia after radiotherapy, the EORTC score can be used to measure hyposalivation. Reduced susceptibility of *C. albicans* might introduce complications to therapy. Findings of more non-*albicans* strains show a change in colonization which should be examined in further studies.

**Keywords** Radiation therapy · Saliva flow rate · *Candida* colonization · Antifungal therapy

## Introduction

Adjuvant and neoadjuvant radiotherapy of head and neck tumors is a fundamental part of the multidisciplinary therapy for head and neck malignancies [14]. For resectable oral squamous cell carcinoma, primary surgery combined with radiation is traditionally considered the approach offering the best opportunity of cure [4]. Indications are locally advanced T3/4 tumors or recurring tumors, evidence of local lymphnode metastasis, tumor growth over the resection limitation or lymphangiosis carcinomatosa [3].

One major side effect of radiotherapy is dysfunction of the salivary glands, dependent upon inclusion of the parotid glands within the radiation field [34, 40]. This leads to a lower salivary flow rate which is associated with a conspicuous impairment of quality of life [1, 17].

Patients undergoing radiation therapy are also predisposed to candidal colonization of the oral mucosa [2, 27].

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Grötz et al. found the maximum oral candidal colonization occurred 6 months after radiotherapy with slightly lower colonization rates after 12 months [17].

*Candida albicans* as a common colonizer of the oral mucosa can cause mild to severe lesions in these patients. However, a temporal shift of the species of yeast isolated from the oral cavities of patients to non-*albicans* species, such as *Candida glabrata* [29], *Candida famata*, *Candida tropicalis*, *Candida dubliensis*, and *Candida krusei* seems to occur after head and neck radiation [28, 37]. Prevention of oral candidal colonization or treatment of *Candida* infections are two of the principal duties for physicians during and after radiation therapy. Hyposalivation as well as candidal colonization are common side effects after radiation therapy. The relationship of hyposalivation and *Candida* colonization after radiation therapy in the long term is not yet described in the literature.

The aim of this study was to evaluate a possible correlation between saliva flow rate, the score for late radiation damage on dental hard tissue (Radiation Therapy Oncology Group (RTOG) scale), the subjective xerostomia rating by the physician (European Organization for Research and Treatment of Cancer (EORTC) scale), and the fungal colonization of the oral cavity in patients after radiation therapy, as well as testing susceptibility to the identified candidal strains.

## Materials and methods

All patients who took part in the study had a multimode therapy with consecutive enrolment for head and neck cancer with surgery and radiation therapy. They were screened at the Department for Oral and Maxillofacial Surgery, University Medical Center of the Johannes Gutenberg-University of Mainz, Mainz, Germany in the routine recall for patients with tumors from March 2006 to February 2008. All investigations and diagnostic procedures were carried out by the same physician. Inclusion criteria for this diagnostic, non-interventional study were: history of oral carcinoma, surgical and radiation therapy, time interval from start of radiation therapy >180 days (exclusion of early radiation side effects [8]), radiotherapy volume including the lower jaw, the total submandibular region and the salivary glands, and the cranial border of the radiation field being above the chin-mastoid plane [23]. All patients routinely underwent surgical and conservative teeth rehabilitation in the planning phase of radiotherapy. Patients who underwent parotidectomy or had been treated with a medication which could lead to reduction of the salivary function were excluded from this study in order to confine the reduction of reduced salivary function to the radiation therapy.

The objective salivary flow rate was measured with sialometry expressing the quantitative level of salivary dysfunction. Sialometry was performed in accordance with the method described earlier [19] and used by other groups [6, 25]. The unstimulated saliva flow rate (SFR) was evaluated by collecting the saliva over 5 min in a quiet room outside the medical ambulance between 09.00 a.m. and 01.00 p.m. If present, the amount of foam was consequently recorded together with the liquid.

According to the measured rates, the SFR were divided into three groups [26]:

- hyposalivation grade I (unstimulated whole saliva flow rate=0.1–0.25 ml/min)
- hyposalivation grade II (unstimulated whole saliva flow rate=≤0.1 ml/min)
- hyposalivation grade III (unstimulated whole saliva flow rate=0.0 ml/min)

An oral assessment was performed for each patient, including the determination of the following parameters: the oral hygiene status, number of teeth, presence of prosthetic appliances, smoking and drinking habits, periodontal conditions using the periodontal screening index (PSI) [9], and presence of plaque using the periodontal plaque index (PI) [36].

The RTOG score for late radiation damage on dental hard tissue ("radiation caries") [18] (Table 1) and RTOG–EORTC scoring system for late radiation-induced morbidity of the salivary glands were recorded [8] (Table 2).

After determination of the saliva flow rate, 2 ml sodium chloride was used to rinse the mouth for 20 s for the semiquantitative determination of the *Candida* counts [32]. Yeasts were isolated from clinical specimens using Sabouraud agar (Oxoid Ltd, Basingstoke, England, UK) and CHROMagar™ Candida (CHROMagar Microbiology, Paris, France). The presence of yeast elements (hyphae, pseudohyphae, and budding yeast) in saliva and the associated confluent yeast growth in colony forming units (cfu) from the oral rinse specimen were the laboratory criteria for yeast colonization. *Candida* species were identified using the API 20 C AUX yeast identifi-

**Table 1** The RTOG score for late radiation damage on dental hard tissue ("radiation caries") [18]

| RTOG score | Clinical findings |
|---|---|
| RTOG 0 | No change in comparison with starting point |
| RTOG I | Plane, chalky staining, loose of the transparency of cement |
| RTOG II | Undercutting caries under the cement |
| RTOG III | Loose of the cement and softening of the dentin |
| RTOG IV | Total damage of the crown |

**Table 2** RTOG–EORTC scoring system for late radiation-induced morbidity of the salivary glands [8]

| EORTC score | Clinical findings |
|---|---|
| EORTC 0 | No changes |
| EORTC I | Diffuse erythema, mild mouth dryness, slightly thickened saliva, slightly altered taste such as metallic taste, feeding behavior, such as increased use of liquids with meals |
| EORTC II | Development of small foci of ulcers, moderate to complete dryness, thick, sticky saliva, markedly altered taste |
| EORTC III | Painful ulcerations extending on more than half of the oral mucosa and, or acute salivary gland necrosis |
| EORTC IV | Fibrosis |

cation system (BioMerieux, Maecy l'Etoil, France). Resistance of the *Candida* species to amphotericin B, and the azole ketoconazole, voriconazole, and fluconazole was examined by using Etest®.

## Statistical analysis

Data collection, data management, and data analysis were performed with statistical software package SPSS® version 16. The continuous parameters were descriptively analyzed. Values were given as mean and standard deviation. The Mann–Whitney test was used to test for possible statistical significance. A $p$ value <0.05 was considered as statistically significant. The study protocol was approved by the local ethics committee (873.205.06 (5303)) and written informed consent was obtained for each patient.

## Results

Fifty three patients (36 males, 17 females) were included with the median age of patients being 60 years (range, 34–84 years). All patients had a head and neck radiation of 50–70 Gy in fractions of 2±Gy per day after surgical tumor therapy (Table 3). The site of cancer were: carcinoma of the tongue in 16 patients (30%), anterior floor of the mouth in 15 patients (28%), alveolar ridge in 7 patients (13%), mandibular angle in 5 patients (9%), palate in 4 patients (8%), upper jaw in 3 patients (6%), velum in 1 patient (2%), inferior lip in 1 patient (2%), and maxillary antrum also in 1 patient (2%).

On average, the radiation therapy was completed 13 months before examination (ranging from 6 to 110 months; first quartile, 9 months; third quartile, 45 months). Thirteen edentulous (25%) and 40 (75%) partly edentulous patients have been examined.

The unstimulated SFR revealed a hyposalivation grade I in 12 (23%) patients, hyposalivation grade II in 14 (26%) patients, and hyposalivation grade III in 27 (51%) patients (Table 3).

No significance between SFR and PI, PSI, RTOG late radiation damage on dental hard tissue score could be

**Table 3** Radiation dose, remaining teeth (edentulous/partly edentulous), dental and periodontal findings (PI/PSI/RTOG caries score) in relation to salivary flow rates (partly edentulous patients) expressed in range and first (Q1) and third quartile (Q3)

| | | Hyposalivation grade I ($n$=12) | Hyposalivation grade II ($n$=14) | Hyposalivation grade III ($n$=27) |
|---|---|---|---|---|
| Radiation dose ($n$=53) | Gy | 60 | 60 | 60 |
| | | [Q1, 59; Q3, 69] | [Q1, 60; Q3, 62] | [Q1, 59; Q3, 64] |
| Teeth ($n$=53) | Edentulous | 3 (6%) | 1 (2%) | 9 (17%) |
| | Partly edentulous | 9 (17%) | 13 (25%) | 18 (34%) |
| PI ($n$=40) | Grade 0 | 2 (5%) | 3 (8%) | 3 (8%) |
| | Grade I | 2 (5%) | 5 (13%) | 5 (13%) |
| | Grade II | 3 (8%) | 5 (13%) | 7 (18%) |
| | Grade III | 2 (5%) | 0 | 3 (8%) |
| | Grade IV | 0 | 0 | 0 |
| PSI ($n$=40) | Grade 0 | 2 (5%) | 2 (5%) | 2 (5%) |
| | Grade I | 3 (8%) | 3 (8%) | 3 (8%) |
| | Grade II | 3 (8%) | 5 (13%) | 8 (20%) |
| | Grade III | 1 (3%) | 3 (8%) | 4 (10%) |
| | Grade IV | 0 | 0 | 1 (3%) |
| RTOG caries ($n$=40) | Grade 0 | 4 (10%) | 4 (10%) | 9 (23%) |
| | Grade I | 3 (8%) | 6 (15%) | 4 (10%) |
| | grade II | 2 (5%) | 3 (8%) | 2 (5%) |
| | grade III | 0 | 0 | 3 (8%) |
| | grade IV | 0 | 0 | 0 |

found. However, a significant correlation between SFR and EORTC for late radiation-induced morbidity of the salivary glands could be detected (Mann–Whitney test, $p=0.001$; Table 4). Smoking and drinking habits showed no influence on SFR (Table 4).

Forty seven *Candida* isolates could be detected in 44 out of the 53 patients (83%; Table 5). Patients showed colonization with different *Candida* species. Overall, 20 (45%) *C. albicans* and 27 (57%) non-*albicans* species were identified. In 30 (68%) of the identified *Candida* species, a probability of API over ≥90% was detected (Table 5). Of the 44 patients with *Candida* carriage, 41 patients (93%) have been colonized with only one species. Carriage of two yeast species was found in the remaining three patients (7%): *C. krusei* and *Sacharomyces cerevisiae* and *Candida parapsilosis* and *Saccharomyces cerevisiae* in two patients with hyposalivation grade II, *Candida zeylanoides* and *C. albicans* in a patient with hyposalivation grade III. There was no relationship between *Candida* colonization and PI, PSI, RTOG late-radiation damage on dental hard tissue score, EORTC oral mucositis score, and smoking and drinking habits. However, a significant correlation between SFR and *Candida* affection could be detected (Mann–Whitney test, $p=0.031$; Table 4).

Out of all 53 patients, 12 (23%) had hyposalivation grade I and of these, 7 (13%) had *Candida* colonization with a mean of $9.1\times10^1$ cfu (range, 200–5,900 cfu); 14 (26%) had hyposalivation grade II and of these, 13 (25%) had *Candida* colonization with a mean of $4.3\times10^1$ cfu (range, 110–3,300 cfu); and 27 (51%) had hyposalivation grade III and of these, in 25 (46%) had *Candida* colonization with a mean of $2.0\times10^3$ cfu (range, 300–19,475 cfu). Spearman's correlation coefficient was −0.245 ($p=0.077$).

The mean minimal inhibition concentration (MIC) of the 20 *C. albicans* strains was 0.38 μg/ml for amphotericin B (range, 0.38–0.50 μg/ml), 17.5 μg/ml (range, 0.41–32.00 μg/ml) for ketoconazole, 32.00 μg/ml (range, 8.38–32.00 μg/ml) for voriconazole, and 256.00 μg/ml (range, 3.25–256.00 μg/ml) for fluconazole. The mean MIC for the 27 non-*albicans* species was 0.50 μg/ml for amphotericin B (range, 0.38–0.75 μg/ml), 3.00 μg/ml (range, 0.45–32.00 μg/ml) for ketoconazole, and 0.50 μg/ml (range, 0.06–32.00 μg/ml) for voriconazole, and 28.00 μg/ml (range, 3.25–256.00 μg/ml) for fluconazole (Table 6).

## Discussion

A correlation between a higher hyposalivation grade and an increased candidal colonization as well as a higher EORTC score for late radiation-induced morbidity of the salivary glands could be detected. In the saliva of the patients, more non-*albicans* species with higher susceptibility to the tested antimicrobial agents than *C. albicans* strains could be found.

Gland function gradually decreases as the radiation doses increase from 20 to 40 Gy, with a strong reduction

**Table 4** Radiation dose, remaining teeth (edentulous/partly edentulous), EORTC saliva score, smoking behavior, drinking behavior, and *Candida* affection with *C. albicans* or non-*albicans* strains in relation to salivary flow rates (all patients) expressed in range and first (Q1) and third quartile (Q3)

| | | Hyposalivation grade I ($n=12$) | | Hyposalivation grade II ($n=14$) | | Hyposalivation grade III ($n=27$) | |
|---|---|---|---|---|---|---|---|
| Radiation dose ($n=53$) | Gy | 60 | | 60 | | 60 | |
| | | [Q1, 59; Q3, 69] | | [Q1, 60; Q3, 62] | | [Q1, 59; Q3, 64] | |
| Teeth ($n=53$) | Edentulous | 3 (6%) | | 1 (2%) | | 9 (17%) | |
| | Partly edentulous | 9 (17%) | | 13 (25%) | | 18 (34%) | |
| EORTC saliva ($n=53$) ($p=0.001$) | Grade 0 | 1 (2%) | | 0 | | 0 | |
| | Grade I | 6 (11%) | | 2 (4%) | | 0 | |
| | Grade II | 5 (9%) | | 12 (23%) | | 12 (23%) | |
| | Grade III | 0 | | 0 | | 15 (28%) | |
| | Grade IV | 0 | | 0 | | 0 | |
| Smoking ($n=53$) | Nonsmoking | 11 (21%) | | 13 (25%) | | 23 (43%) | |
| | Smoking | 1 (2%) | | 1 (2%) | | 4 (8%) | |
| Alcohol ($n=53$) | Never | 4 (8%) | | 9 (17%) | | 13 (25%) | |
| | Moderate | 5 (9%) | | 4 (8%) | | 10 (19%) | |
| | Daily | 3 (6%) | | 1 (2%) | | 4 (8%) | |
| *Candida* ($n=53$) ($p=0.031$) | No *Candida* | 5 (9%) | | 1 (2%) | | 3 (6%) | |
| | *Candida* | 7 (13%) | | 13 (25%) | | 24 (45%) | |
| | | *C. albicans* 4 (8%) | Non-*albicans* 3 (6%) | *C. albicans* 6 (11%) | Non-*albicans* 7 (13%) | *C. albicans* 10 (19%) | Non-*albicans* 14 (26%) |

**Table 5** Distribution of the 47 *Candida* strains in 44 affected patients and their probability of identification using API AUX 20C

| API | *C. albicans* *n*=20 | *C. glabrata* *n*=5 | *C. famata* *n*=8 | *C. tropicalis* *n*=5 | *C. parapsilosis* *n*=1 | *C. dubliensis* *n*=1 | *C. lusitanae* *n*=1 | *C. krusei* *n*=1 | *C. zelanoides* *n*=1 | *S. cerevisiae* *n*=4 |
|---|---|---|---|---|---|---|---|---|---|---|
| <80% | 3 | 0 | 5 | 5 | 0 | 0 | 1 | 0 | 0 | 0 |
| 80–89.9% | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 90–98.9% | 8 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 2 |
| 99–99.8% | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| >99.9% | 0 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |

In all three patients with two different *Candida* strains, only non-*albicans* strains could be found

at over 40 Gy [5]. Roesink et al. showed a reduction in saliva function as a short-term side effect with a tendency to recover over time [31]. Grötz et al. showed that this slight recovery of salivary function can take place in the first 12 months after radiotherapy but did not lead to normal function [17]. The detection of hyposalivation grade III in over 50% of the patients after radiation therapy with 50–70 Gy is related with the loss of up to 90% of acinar cells [20] and an increase of the extracellular extravascular space and decreased vascular permeability [21]. Not a single patient had normal SFR, which underlines the reduced function of the salivary glands after radiation therapy as a long-term radiation effect.

The oral hygiene status measured with RTOG late radiation damage on the dental hard tissue score, PI, and PSI showed no correlation with the occurrence of hyposalivation. Contrary to these findings, Eliasson et al. found in patients after radiation therapy with a lower saliva flow rate (<0.1 ml/min) a correlation between increased acidogenic plaque and saliva buffer capacity, although mostly in unrestored teeth [11]. The difference with the patients' collective of the studies might be explained by the group of edentulous and partly edentulous patients, since these patients might have benefited from preventive treatment such as surgical and conservative teeth rehabilitation before radiation therapy.

There was no correlation between hyposalivation and the smoking and drinking habits in this study, although a correlation has previously been described between xerostomia, the objective feeling of a dry mouth, and smoking in a longitudinal study in a Swedish population [15]. However, only a limited comparison between the study results are possible because the patients in the study of Field et al. showed xerostomia due to Sjögren's syndrome and other underlying diseases [15].

The EORTC score for late radiation-induced morbidity of the salivary glands was the only clinical parameter that showed a correlation to the occurrence of hyposalivation. The incidence of oral candidiasis and oral colonization with *Candida* species during and after radiation therapy, which has been reported in different studies, shows a wide variation, ranging between 17% and 86% [12, 22, 30, 38]. In healthy participants, a range of 20–45% [38, 41] *Candida* colonization has been described. Using the mouth wash method, a range of up to 600 cfu can be detected in clinical inconspicuous patients [24]. In the study, the highest quantity of cfu was found in the group of patients with hyposalivation grade III; however, there was no significance between the groups. The high incidence of 83% of *Candida*-affected patients causes concern since the cancer patients are immunocompromised individuals and more susceptible to opportunistic fungal infections which rarely cause disease in healthy subjects [16]. Even though the candidal colonization was determined in the study, it cannot be compared with *Candida* infection of the patients.

The coherence of smoking and candidal colonization in the literature has not been consistently assessed. Epstein et al. found a correlation between xerostomia after radiation therapy, smoking and drinking habits, and candidiasis [12]. However in the study of Ramirez-Amador et al., smoking and denture wearing were not statistically signif-

**Table 6** Mean susceptibility and range of 20 *Candida albicans* strains and 27 non-*albicans* strains against amphotericin B, ketoconazole, fluconazole, and voriconazole tested with Etest

| Antifungal agent | | Amphomtericin B | Ketoconazole | Voriconazole | Fluconazole |
|---|---|---|---|---|---|
| Highest conc. of the Etest (μg/ml) | | 32.00 | 32.00 | 32.00 | 256.00 |
| *C. albicans* (*n*=20) | Average range | 0.38 [0.38, 0.50] | 17.50 [0.41, 32.00] | 32.00 [8.38, 32.00] | 256.00 [3.25, 256.00] |
| Non-*albicans* (*n*=27) | Average range | 0.50 [0.38, 0.75] | 3.00 [0.45, 32.00] | 0.50 [0.06, 32.00] | 28.00 [3.25, 256.00] |

icant risk factors for increased candidal colonization under radiation therapy [27]. In comparison, smoking and drinking habits represent no increased risk for oral candidal colonization after radiation therapy in this study.

Likewise, no correlation of the partly edentulous patient's caries score (RTOC caries), the PI and PSI could be shown with concomitant yeast colonization. Regardless, lower saliva flow rates correlate with a higher risk for *Candida* affection in patients after radiation therapy. Torres et al. described controversial results in a collective of 133 patients with different diseases, whereby no correlation was found between lower salivary flow rates and *Candida* colonization of all yeasts. However, a relationship between low salivary flow rates and higher unit counts was observed in certain colony forming yeasts, namely, *C. albicans* and *C. parapsilosis*. In comparison with this study, the study of Torres et al. relied on higher median salivary flow rates. Another difference of the present study to Torres et al. is that all patients shared the same disease, details about the radiation therapy are provided and a correlation between saliva flow rates and *Candida* colonization was found [39].

A bias of this study might be the wide time range of 6–110 months between radiation therapy and the examination of the SFR.

Grötz et al. could show that there is a change of the *Candida* amount after radiation therapy over time with a reduction after 12 months in a follow up which was not examined in the study [17].

In the past, *C. albicans* was the most common organism isolated from orapharyngeal candidiasis. Non-*albicans* strains have been cultured from these patients but were thought to be colonizing organisms and not a significant cause of disease. Examination in patients with human immunodeficiency virus showed species other than albicans causing oropharyngeal infections [33]. The prevalence of *C. albicans* and other yeasts from the oropharynx in patients of the study receiving radiation for head and neck cancer varies. In addition to *C. albicans*, many non-*albicans* species have been isolated in the saliva of cancer patients [2, 10]. The predominant non-*albicans* strains in the study have been *C. famata*, *C. glabrata*, and *C. tropicalis*.

*C. albicans* strains have the highest in vitro susceptibility against amphotericin B. Testing the azole group of antifungal agents' *C. albicans* have been resistant to the highest concentration of the Etest of voriconazole and fluconazole and have also shown a resistance to ketoconazole but not to the highest concentration of the Etest. Similar results could be shown by Fadda et al. whereby over a 3-year period, 472 *Candida* species were isolated from patients hospitalized either in Bone Marrow Transplant Unit and Intensive Care Unit or in conventional wards of the Pneumological Divisions of the "Binaghi" Hospital of Cagliari [13].

Non-*albicans* strains showed, in vitro, in all tested antifungal agents, a higher susceptibility than *C. albicans* strains; however, testing fluconazole the susceptibility was lower with 28.00 μg/ml but still less than the *C. albicans* strains.

Fluconazole has emerged as a popular medication to treat *Candida* infections in patients after radiation therapy. However, the development of resistance to fluconazole has become a growing concern and is usually correlated with the degree of immunosuppression of the patients and the total drug dose. The description of resistance mechanism in gene mutations of *C. albicans* against fluconazole is of great interest and well described [7, 35].

## Conclusions

As a long-term effect, hyposalivation can occur in patients after radiation therapy in the head and neck region. Dependent on the value of hyposalivation, a higher oral candidal colonization must be expected. The EORTC score for late radiation-induced morbidity of the salivary glands is an instrument for testing the subjective development of hyposalivation. In addition to *C. albicans*, an even higher number of non-*albicans* strains could be verified in the saliva of the patients. The susceptibility of *C. albicans* was lower than the non-*albicans* strains. Ampothericin B proved to be the most effective of the tested antifungal agents.

**Conflict of interest** The authors declare that they have no conflict of interest.

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