

# Tooth loss and implant outcomes in patients refractory to treatment in a periodontal practice

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## Abstract

**Aim:** The aim of this study was to investigate the factors associated with continued significant tooth loss due to periodontal reasons during maintenance following periodontal therapy in a specialist periodontal practice in Norway.

**Material and Methods:** A case–control design was used. Refractory cases were patients who lost multiple teeth during a maintenance period of 13.4 (range 8–19) years following definitive periodontal treatment in a specialist practice. Controls were age- and gender-matched maintenance patients from the same practice. Characteristics and treatment outcomes were assessed, and all teeth classified as being lost due to periodontal disease during follow-up were identified. The use of implants in refractory cases and any complications relating to such a treatment were recorded.

**Results:** Only 27 (2.2%) patients who received periodontal treatment between 1986 and 1998 in a specialist practice met the criteria for inclusion in the refractory to treatment group. Each refractory subject lost 10.4 (range 4–16) teeth, which represented 50% of the teeth present at baseline. The rate of tooth loss in the refractory group was 0.78 teeth per year, which was 35 times greater than that in the control group. Multivariate analysis indicated that being in the refractory group was predicted by heavy smoking ( $p = 0.026$ ), being stressed ( $p = 0.016$ ) or having a family history of periodontitis ( $p = 0.002$ ). Implants were placed in 14 of the refractory patients and nine (64%) of these lost at least one implant. In total, 17 (25%) of the implants placed in the refractory group were lost during the study period.

**Conclusions:** A small number of periodontal maintenance patients are refractory to treatment and go on to experience significant tooth loss. These subjects also have a high level of implant complications and failure. Heavy smoking, stress and a family history of periodontal disease were identified as factors associated with a refractory outcome.

Key words: implant failure; outcomes; periodontal disease; refractory patients; risk factors; tooth loss

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Periodontal therapy carried out in specialist practice is successful in maintaining the majority of patients' teeth over time (Fardal et al. 2004). A small

proportion of patients continue to suffer from progressive periodontal deterioration in spite of regular maintenance. The term refractory periodontal disease has been applied to such individuals who are characterized by continued degeneration of the periodontium despite ongoing sanative, surgical and/or pharmacological therapy (American Academy of Periodontology 2000). There has been considerable discussion about whether refractory periodontitis represents a

separate entity because of the difficulty in distinguishing between refractory and recurrent periodontal disease (Armitage 2002). Research studies have highlighted factors such as changes in the subgingival microflora and/or the host response, which might be associated with the progression of periodontitis in well-maintained patients. Haffajee et al. (2004) have suggested that refractory periodontitis may represent a state in which the clinician and the patient are

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unable to lower the infectious bacterial burden below a level that can be tolerated by the host's innate and acquired resistance and environmental status.

In a practical sense, however, periodontists are faced with patients who do not respond to conventional therapy. Ultimately, it is tooth loss as a result of progressive periodontitis that will prove to be the problem that has to be faced by both affected patients and their dentists. In this context, limited information exists on periodontal maintenance patients who continue to lose teeth to such an extent that major prosthetic replacements are required. A number of studies have reported complications when implants were used in patients with a history of progressive periodontal disease (Hardt et al. 2002, Karoussis et al. 2003, Roos-Jansåker et al. 2006).

The classic study of Hirschfeld and Wasserman (1978) used tooth loss during long-term maintenance as the outcome measure for the success of periodontal therapy, with failing patients being classified as "downhill" (loss of four to nine teeth) or "extreme downhill" (loss of 10 or more teeth). It is not known what proportion of long-term maintenance patients are unresponsive to treatment to the extent that they lose multiple teeth, the distribution of tooth loss, predisposing factors or the outcomes of the replacements for the lost teeth in such patients. The aim of the current study was to identify factors associated with significant tooth loss due to periodontal reasons during maintenance in patients who received periodontal therapy in a specialist periodontal practice. The outcome of implant therapy in these cases was also studied. This study was one of a series that aimed to develop internal quality control measures that could be applied to specialist periodontal practices (Fardal et al. 2001, 2002).

## Material and Methods

### Study population

All patients attending the principle investigator (Ø. F.), a specialist certified by the Norwegian Department of Health and Social Services, for periodontal maintenance therapy between July 2003 and August 2006 were screened for possible inclusion in the study. The specialist practice receives referrals from general dental practitioners, community dentists

and physicians in a Norwegian rural community. The area has approximately 25 dentists split evenly between private practice and the community dental service. The patients were mainly Northern Europeans and drawn from small rural Norwegian communities.

The inclusion criteria for cases were that they were patients who received initial periodontal therapy, followed by at least 8 years of maintenance treatment in the specialist practice and who lost multiple teeth during the maintenance period, such that they were classified as downhill (lost four to nine teeth) or extreme downhill (lost 10 or more teeth) as defined by Hirschfeld and Wasserman (1978). In addition, the loss of teeth was not part of an initial treatment plan to extract hopeless teeth. All patients treated in the practice since it opened in 1986, who met the inclusion criteria, were enrolled in the study. The maintenance therapy in the specialist practice was shared between three hygienists and the investigator (Ø. F.). The controls were age- and gender-matched patients who attended the specialist practice for treatment and maintenance over the same period. Two controls were chosen as a representative convenience sample from the practice database for each case.

Gender, date of birth, medical history including drug history at the time of the initial visit to the practice for diagnosis and treatment planning were obtained from the clinical records for all participants. Each participant was questioned at the initial visit on whether they considered they were suffering from stress and whether they were currently taking or had taken antidepressants. At the same visit, each participant was questioned in detail about whether close relatives (parents, children, brothers or sisters) had a history of periodontal disease. Unless the relative was a patient in the specialist office, the family history was not verified by examination of the relative. Smoking habits of all cases and controls were recorded in terms of the numbers of cigarettes smoked per day. Heavy smoking was equated to consumption of 20 or more cigarettes per day. Patients who smoked only on social occasions were not classified as smokers. The diagnosis of periodontal disease and subsequently the type of definitive periodontal therapy (non-surgical and/or surgical) were recorded. At the first visit for maintenance following initial definitive periodontal therapy,

a prognosis of good, uncertain or poor, based on the clinical judgement of the periodontist (Ø. F.), was recorded for each patient. The prognosis took into account the periodontal support of remaining teeth, healing after periodontal therapy, assessed level of plaque control, smoking habits, reported family history of periodontal disease and other systemic periodontal risk factors. The average levels of plaque control during maintenance (good, moderate, poor) as outlined by Fardal and Linden (2005) and compliance with maintenance therapy (complete, erratic) were noted.

At the final assessment, the type of prosthetic treatment carried out to replace lost teeth was recorded. The use of implants and any complications relating to implant treatment such as non-integration, peri-implantitis or loss of implants were recorded from the clinical notes.

In addition, where relevant, patients were asked how satisfied they were with the implant and prosthetic therapy they received to replace their lost teeth.

### Tooth loss

During the follow-up period, all tooth loss was monitored. Teeth that were extracted due to root fracture, deep carious lesions that rendered the tooth non-restorable or because of the failure of endodontic therapy were considered non-periodontal extractions. All teeth classified as being lost due to periodontal disease were identified.

### Statistical analysis

Student's *t*-test or  $\chi^2$  analysis was used, with the level of significance set at  $p < 0.05$ . Multivariate analysis was carried out using logistic regression to identify possible predictors of tooth loss during the period of review.

## Results

A total of 27 (17 female, 10 male) out of 1251 patients (2.2%) who received initial periodontal treatment between 1986 and 1998 met the criteria for inclusion in the downhill/extreme downhill refractory group. The average age of these patients at their initial examination was 48.5 (SD 10.0, range 21–71) years, and they had on average 20.6 (SD 4.6, range 13–28) teeth. The majority [23 (85%)] of the refractory group were compliant

Table 1. Comparison between refractory and control subjects

|   | Refractory  | Control     | <i>p</i> -value |
|---|-------------|-------------|-----------------|
| Age initial assessment, mean (SD)                       | 48.5 (10.0) | 48.1 (10.2) | 0.86            |
| Years in maintenance since treatment started, mean (SD) | 13.4 (3.3)  | 13.9 (3.2)  | 0.50            |
| Teeth present at start of treatment, mean (SD)          | 20.6 (4.6)  | 25.8 (2.6)  | <0.0001         |
| No. of teeth lost during monitoring period, mean (SD)   | 10.4 (3.75) | 0.3 (0.57)  | <0.0001         |
| Smoking, <i>n</i> (%)                                   |             |             |                 |
| Non-smokers   | 11 (40.7)   | 39 (72.2)   |                 |
| Light   | 5 (18.5)    | 10 (18.5)   |                 |
| Heavy   | 11 (40.7)   | 5 (9.3)     | 0.0026          |
| Systemic disease, <i>n</i> (%)                          | 8 (29.6)    | 17 (31.5)   | 0.86            |
| Hygiene, <i>n</i> (%)                                   |             |             |                 |
| Good  | 11 (40.7)   | 22 (40.7)   |                 |
| Moderate  | 11 (40.7)   | 31 (57.4)   |                 |
| Poor  | 5 (18.5)    | 1 (1.9)     | 0.02            |
| Stress, <i>n</i> (%)                                    | 11 (40.7)   | 1 (1.9)     | <0.0001         |
| Family history of periodontitis, <i>n</i> (%)           | 19 (70.4)   | 13 (24.1)   | <0.0001         |

Table 2. Distribution of tooth loss in the refractory group by tooth type and arch

|       |   |    |    |    |    |    |    |    |    |    |    |    |    |   |    |
|-------|---|----|----|----|----|----|----|----|----|----|----|----|----|---|----|
| Upper | 9 | 12 | 11 | 13 | 11 | 19 | 15 | 13 | 16 | 16 | 16 | 10 | 13 | 6 | 1  |
|       | 8 | 7  | 6  | 5  | 4  | 3  | 2  | 1  | 1  | 2  | 3  | 4  | 5  | 6 | 7  |
| Lower | 1 | 11 | 7  | 7  | 6  | 3  | 7  | 8  | 7  | 7  | 5  | 4  | 4  | 9 | 13 |

In total, 280 teeth were lost.

with the maintenance regimens prescribed, while four (15%) showed erratic compliance. The average period of monitoring the refractory group was 13.4 (SD 3.3, range 8–19) years.

The refractory subjects started treatment at the same age and had been under specialist care for the same time as the controls (Table 1). There was good plaque control in 41% of both the refractory and the control subjects (Table 1). A higher proportion of the refractory (19%) than the control (2%) subjects had poor oral hygiene (Table 1). The subjects in the refractory group had on average five teeth less than those in the control group at the start of treatment. In total, seven teeth were removed between the initial examination and the start of maintenance therapy in the refractory group and two teeth were removed in the control group. There was no difference in the proportion of each group that had periodontal surgery: 93% of refractory compared with 96% of the control group. The case prognosis after the initial definitive therapy showed that the refractory group had 25 (93%) patients with uncertain or poor prognosis, which was not significantly different from the control group, which had 42 (78%) patients with uncertain or poor prognosis ( $\chi^2$  2.76,  $p$  = 0.10). On average, each refractory subject lost 10.4 (range 4–16) teeth during the monitoring period, which repre-

sented 50% of the teeth present at the start of the study. The distribution of tooth loss by tooth type and arch in the refractory group is shown in Table 2. The rate of tooth loss in the refractory group was 0.78 teeth per year, which was 35 times greater than that in the control group.

In total, 12 (44%) of the refractory group lost all the teeth in one arch, and a further case became edentulous. Those who became edentulous in one or both arches lost on average 12 (SD 3.3) teeth, which was more than the other refractory cases who lost 8.9 (SD 3.6) teeth ( $p$  = 0.027). There was no difference in the proportion of the refractory or the control group reporting a significant systemic disease or condition (Table 1). Cardiovascular disease, hypertension and diabetes were the main systemic conditions, and these were present in five (19%) of the refractory and 13 (24%) of the control group. It can be seen from Table 1 that a higher proportion of the refractory than the stable group were heavy smokers ( $p$  = 0.0026) or admitted to being severely stressed ( $p$  < 0.0001). A very high proportion (70%) of the refractory group had a close relative with periodontal disease, and this was significantly more than that in the control group ( $p$  < 0.0001). Logistic regression analysis indicated that being in the refractory group was predicted by being a current heavy smoker

( $p$  = 0.026), being stressed ( $p$  = 0.016) or having a family history of periodontitis ( $p$  = 0.002).

#### Implant therapy in refractory cases

Implants were placed in 14 (52%) of the refractory group compared with two (4%) of the control group ( $p$  < 0.0001). Those in the refractory group who received implants lost 8.8 (SD 3.7) teeth, which was less than those who were not treated with implants (12.0, SD 3.2;  $p$  = 0.027). Those treated with implants in the refractory group received an average of 4.9 (SD 2.1) implants. Within the refractory group, there was no difference in the age at assessment of those who were eventually treated with implants compared with those who were not: 50.2 (SD 10.6) compared with 46.7 (SD 9.4) years ( $p$  = 0.37). Within the refractory group, the period in supportive periodontal therapy (SPT) for those who received implants was virtually the same as for non-implant cases: 13.2 (SD 3.9) compared with 13.6 (SD 2.6) years ( $p$  = 0.76). The implants were followed up for on average 5.4 (range 2–9) years. A total of 14 implants in seven refractory patients did not integrate. A further five implants in four patients developed peri-implantitis (one after 3 years, one after 5 years, one after 6 years and two after 8 years), and three of these implants were finally lost (Table 3). In total, 17 (25%) of the implants placed in the refractory group were lost during the study period, and nine (64%) of the refractory group lost at least one implant (Table 3). The two implants placed in the control group showed no complications.

The implant cases in the refractory group were restored using four implant-supported fixed bridges (upper jaw) and

Table 3. Implant placement and outcomes for the refractory patient group

|                                       | No. of implants, <i>n</i> (%) | No. of patients, <i>n</i> (%) |
|---------------------------------------|-------------------------------|-------------------------------|
| Implants placed                       | 68 (100)                      | 14 (100)                      |
| Implants lost due to non-integration  | 14 (21)                       | 7 (50)                        |
| Peri-implantitis                      | 5 (7)                         | 4 (29)                        |
| Implants lost due to peri-implantitis | 3 (4)                         | 2 (14)                        |
| Total no. of implants lost            | 17 (25)                       | 9 (64)                        |

10 fixed bridges (seven upper jaw and three lower jaw), using a combination of teeth and implants for support. The rest of the refractory group of patients were restored using 10 complete dentures, nine removable partial dentures and 11 tooth-supported fixed bridges. Patients' subjective assessments of the prosthetic therapy favoured fixed over removable restorations.

## Discussion

This study investigated a group of patients who, despite comprehensive periodontal treatment, followed by regular supportive periodontal treatment (SPT) in a specialist periodontal practice, continued to lose teeth as a result of progressive periodontitis. It was on the basis of this continued tooth loss that these patients were pragmatically categorized as refractory to treatment, and they formed a very small proportion of the population of patients in active maintenance in the specialist practice. To investigate factors associated with continued tooth loss, a case-control design was used with maintenance patients from the specialist periodontal practice acting as controls. A limitation of the study is that the cases and controls were not matched for disease severity at baseline; however, the prognoses assigned by the clinician were not significantly different for the refractory compared with the control patients. A higher proportion of the refractory than the control group had poor oral hygiene, and this may have affected the progression of periodontitis in some patients. Nevertheless, 41% of both groups had good oral hygiene throughout maintenance, and because less than 20% of the refractory cases were classified with poor oral hygiene, it seems unlikely that differences in plaque control could explain the differences in tooth loss between the groups. The cases were well matched to the controls in relation to age and sex, and both groups had comparable high levels of compliance with the prescribed SPT programme over at least 8 years following definitive periodontal treatment. It has been shown that SPT is a critical factor for long-term successful outcomes following periodontal treatment; nevertheless, subjects with tooth loss resulting from the effects of periodontitis are at an increased risk of further periodontal destruction (Renvert & Persson 2004).

The refractory cases may therefore be at risk, because they had lost more teeth than the controls by the start of the SPT phase, presumably reflecting the effects of periodontitis and the outcome of previous periodontal treatment. The number of teeth removed during definitive periodontal therapy was very low, with seven hopeless teeth being removed in the refractory group, while only two teeth were removed in the control group.

The low level of tooth loss in the control group confirms the findings of previous studies from both private practice (Hirschfeld & Wasserman 1978, Fardal et al. 2004) and University hospital settings (Lindhe & Nyman 1984, Tonetti et al. 2000) that it is possible to maintain a high level of tooth survival after treatment in the majority of patients. Nevertheless, previous long-term studies of the outcomes of periodontal treatment have also identified small numbers of patients who continued to lose a significant number of teeth despite optimal care (Hirschfeld & Wasserman 1978, Lindhe & Nyman 1984, Konig et al. 2002). In the current study, only 2% met the inclusion criteria for the high tooth loss group, which was fewer than that has described in previous studies (Hirschfeld & Wasserman 1978, McFall 1982, Goldman et al. 1986). Various factors may have contributed to the low proportion of refractory cases including a shorter follow-up period in the present study, a high compliance rate with SPT and active re-treatment as part of the maintenance therapy in the practice setting (Fardal et al. 2003, Fardal & Linden 2005). Classic long-term studies of periodontal patients enrolled in maintenance programmes suggest that molars with furcation involvements are the teeth that are most frequently lost (Hirschfeld & Wasserman 1978, McFall 1982). This was not the case in the refractory group in the current study, where the chance of losing a multirooted tooth due to periodontitis was the same as the chance of losing a single-rooted tooth. This probably reflects severe and generalized progressive periodontitis in these patients, leading to loss of all types of teeth. In addition, the refractory cases had lost more teeth before baseline, and this may have been due to early loss of multirooted teeth.

Analysis of exposure variables indicated that heavy smoking, self-reported stress and a family history of perio-

dontal disease were associated with being in the refractory group and therefore with continued tooth loss. To correct for possible confounding, these variables were entered into multivariate analysis. In the final multivariate statistical model, these factors remained significant, suggesting that each had an independent effect. Smoking is a well-known environmental risk factor for poor response to treatment both in the short term (Hughes et al. 2006) and in the long term (Fardal et al. 2004). In the population studied, smoking has previously been shown to be a risk factor for continued tooth loss during periodontal maintenance (Fardal et al. 2004). The relationship between smoking and refractory to treatment periodontal disease agrees with the conclusions of Macfarlane et al. (1992). Stress has been shown to be associated with progression of periodontitis (Linden et al. 1996) and may also influence the outcome of treatment through various mechanisms affecting the host response (Deinzer et al. 2000) as well as patient behaviour (Croucher et al. 1997).

The study relied on information gathered from the participants at their initial examination visit. As a result, the response to questions in relation to risk factors such as smoking is not likely to have been affected by the information supplied by the periodontist on the inter-relationship of various risk factors and periodontitis. The study design did not allow modifications of risk factors such as changes in smoking habits or stress levels during the maintenance period to be considered in the data analysis. Nevertheless, the study did identify factors that, if present before treatment, could help clinicians in their assessment of the possible long-term outcomes of periodontal treatment. It is acknowledged that information on family history is largely dependent on the patients' responses. However, it has been shown that the reliability of periodontal family history is good, particularly when it is positive (Llorente & Griffiths 2006). A family history of periodontitis was reported by a significantly higher proportion of the refractory than the control subjects, supporting a possible association with genetic factors. This was also a risk factor for the re-treatment of periodontal disease in the same clinical setting (Fardal & Linden 2005). There is considerable interest in unravelling the genetic basis of periodontitis, and there has been a major focus on

a possible role for the interleukin-1 (IL-1) composite genotype (see reviews Kinane et al. 2005, Loos et al. 2005). A recent systematic review concluded that there is insufficient evidence to support an association between the IL-1 composite genotype and progressive periodontitis, and therefore the results of testing should be interpreted with caution (Huynh-Ba et al. 2007). In the specific context of the current study, gene expression profiling has identified a number of candidate genes that have altered regulation in refractory periodontitis including upregulation of matrix metalloproteinases 1 and 3 (Kim et al. 2006).

Many of the refractory cases lost a significant number of teeth, resulting in them becoming edentulous in at least one arch. The rate of tooth loss in the patients in the refractory group was 35 times greater than that in the controls and equated to a loss of on average 50% of their remaining teeth. As a result, many of the refractory group required extensive restorative treatment and expressed a high preference for fixed restorations, with over half of the refractory patients being provided with implants. The study was not explicitly designed to investigate the performance of implants in refractory patients, but rather provided an opportunity to study outcomes in subjects who continued to lose teeth despite appropriate periodontal treatment and maintenance. Patients who are refractory to treatment form a very small proportion of those with periodontitis, but are an important group in terms of the provision of multiple implants. There is limited published information to help clinicians faced with such patients so that they can provide rational advice to support patients in making an informed decision as to whether to embark on such treatment.

Studies have shown that in partially dentate patients, the remaining teeth act as a reservoir for the colonization of the subgingival environment related to implants (Quirynen & Teughels 2003, Quirynen et al. 2007), and this may explain in part the poor performance of implants in the refractory patients studied. Hardt et al. (2002) found that subjects classified with periodontitis had a higher 5-year failure rate of implants (8%) than subjects without periodontitis (3.3%). The finding that periodontitis-susceptible subjects had an increased risk of implant failure was supported by Karoussis et al. (2003), who reported a

5-year implant failure rate of 9.5% in periodontitis cases compared with 3.5% in periodontally healthy cases. A further study by Roos-Jansåker et al. (2006) concluded that there was a relationship between implant loss and periodontal bone loss at the time of implant placement and that smoking was an explanatory factor for implant failure. Systematic reviews, however, concluded that there was no difference in implant survival between patients with a history of chronic periodontitis and those who were periodontally healthy (Schou et al. 2006; Karoussis et al. 2007). This may relate to the paucity of studies and the small size of some of the groups studied; for example, there were only eight subjects with periodontitis in the study completed by Karoussis et al. (2003). A recent review by Quirynen et al. (2007) concluded that there was a low risk involved in placing implants in periodontal maintenance patients. However, they also reported that few studies in which confounding factors had been accounted for were available for comparisons.

In the current study, there was a much higher rate of implant failure than the 5-year failure of <10% reported in studies of implants placed in patients with treated periodontal disease (Hardt et al. 2002; Karoussis et al. 2003). At the implant level in the refractory subjects, one-quarter of the implants failed; however, eight of these implants were lost in one patient who formed the basis of a previous report (Fardal et al. 1999). The main complication in the present study was early failure due to a lack of osseointegration. The study was not designed to investigate possible reasons for implant failure, but it may be that factors associated with refractory patients such as heavy smoking and stress were also associated with early implant failure. The impact of implant failure is likely to be more important at the level of the patient. An analysis of outcomes from a patient-centred viewpoint showed that almost two-thirds (64%) of refractory patients who received implants had at least one failure. Roos-Jansåker et al. (2006) reported that implant failures tended to cluster in a small number of patients, and this may reflect the group investigated in the current study that formed a small subgroup of the larger population receiving maintenance in a specialist practice. Nevertheless, the outcomes reported would suggest that implant treatment

should be provided with caution in cases of progressive periodontitis associated with continued tooth loss despite regular SPT.

In conclusion, a small number of periodontal maintenance patients seem to be refractory to treatment and go on to experience continued and significant tooth loss. These subjects also have a high level of implant complications and failure. Smoking, stress and a family history of periodontal disease were identified as factors associated with a refractory outcome, and these variables remained significant after multivariate analysis. In the context of the current study, it is possible that these factors were not only associated with an increased risk of progressive periodontitis and tooth loss but also with an increased likelihood of implant failure.

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### Clinical Relevance

*Scientific rationale for the study:* Some patients are refractory to periodontal therapy and continue to lose teeth despite supportive treatment. Little information exists on factors associated with tooth loss in such refractory patients and how they respond to the replacement of lost teeth with implants.

*Principal findings:* Following definitive treatment, only 2% of main-

tenance patients in a specialist periodontal practice were classified as refractory to treatment, but they lost more than half their remaining teeth over a follow-up of on average 13 years. Heavy smoking, stress and a family history of periodontitis were strongly associated with such tooth loss. Refractory patients had a high rate of complications and failure with implant therapy.

*Practical implications:* Even with high-quality periodontal treatment and appropriate regular supportive therapy, not all patients can be stabilized. A very small proportion continue to lose teeth, and this may be associated with risk factors such as smoking, stress and a family history of periodontitis. Implant treatment should be provided with caution in such cases of progressive periodontitis associated with continued tooth loss.

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