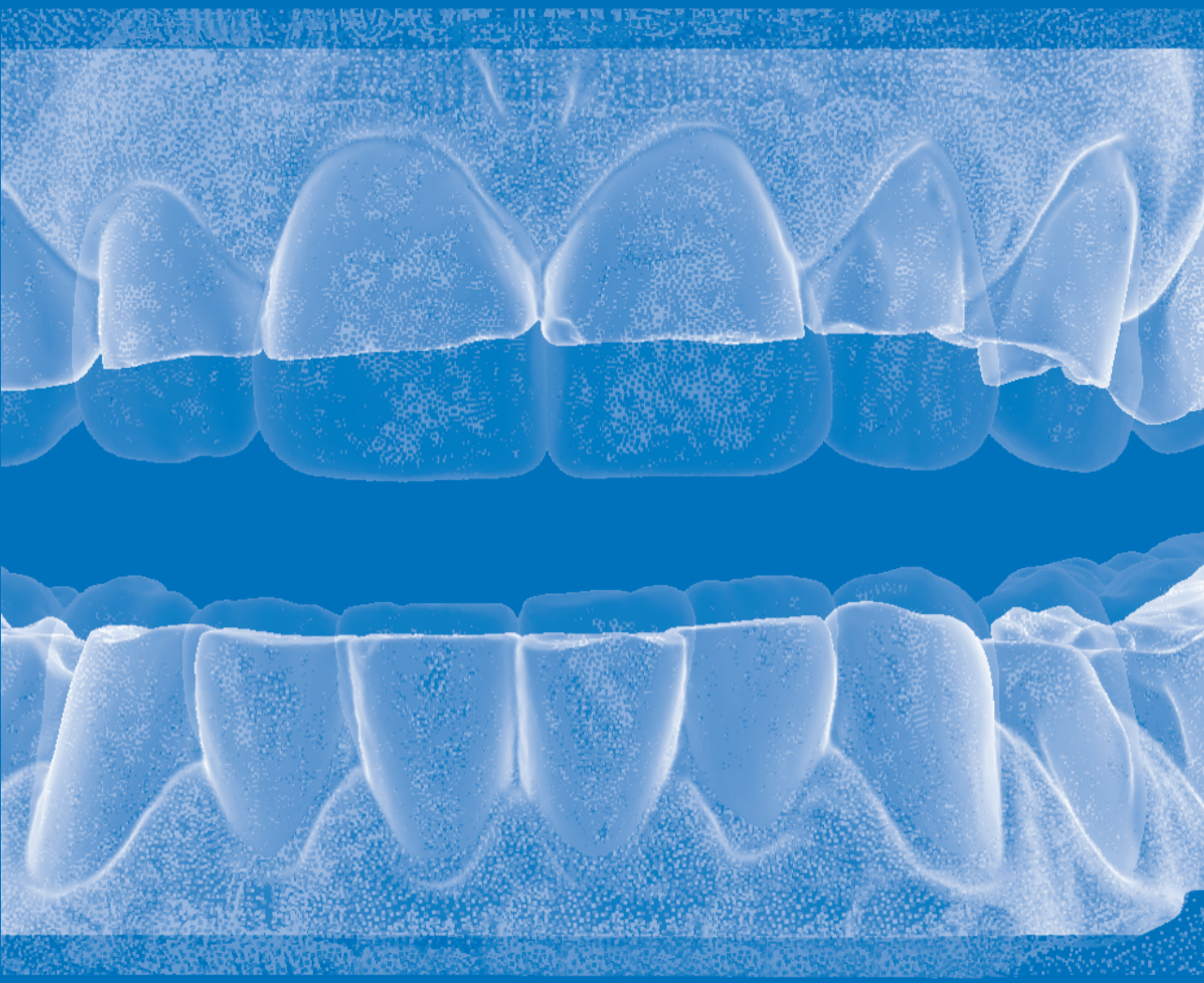

Restorative Management of Tooth Wear

Minimally invasive restorative treatment approaches

Luuk A.M.J. Crins

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Radboudumc

RESTORATIVE MANAGEMENT OF TOOTH WEAR

Minimally invasive restorative treatment approaches

Proefschrift ter verkrijging van de graad van doctor

aan de Radboud Universiteit Nijmegen
op gezag van de rector magnificus prof. dr. J.M. Sanders,
volgens besluit van het college voor promoties
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Paranimfen
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"If I have seen further [than others], it is by standing on the shoulders of Giants."

Isaac Newton, February 5th 1675

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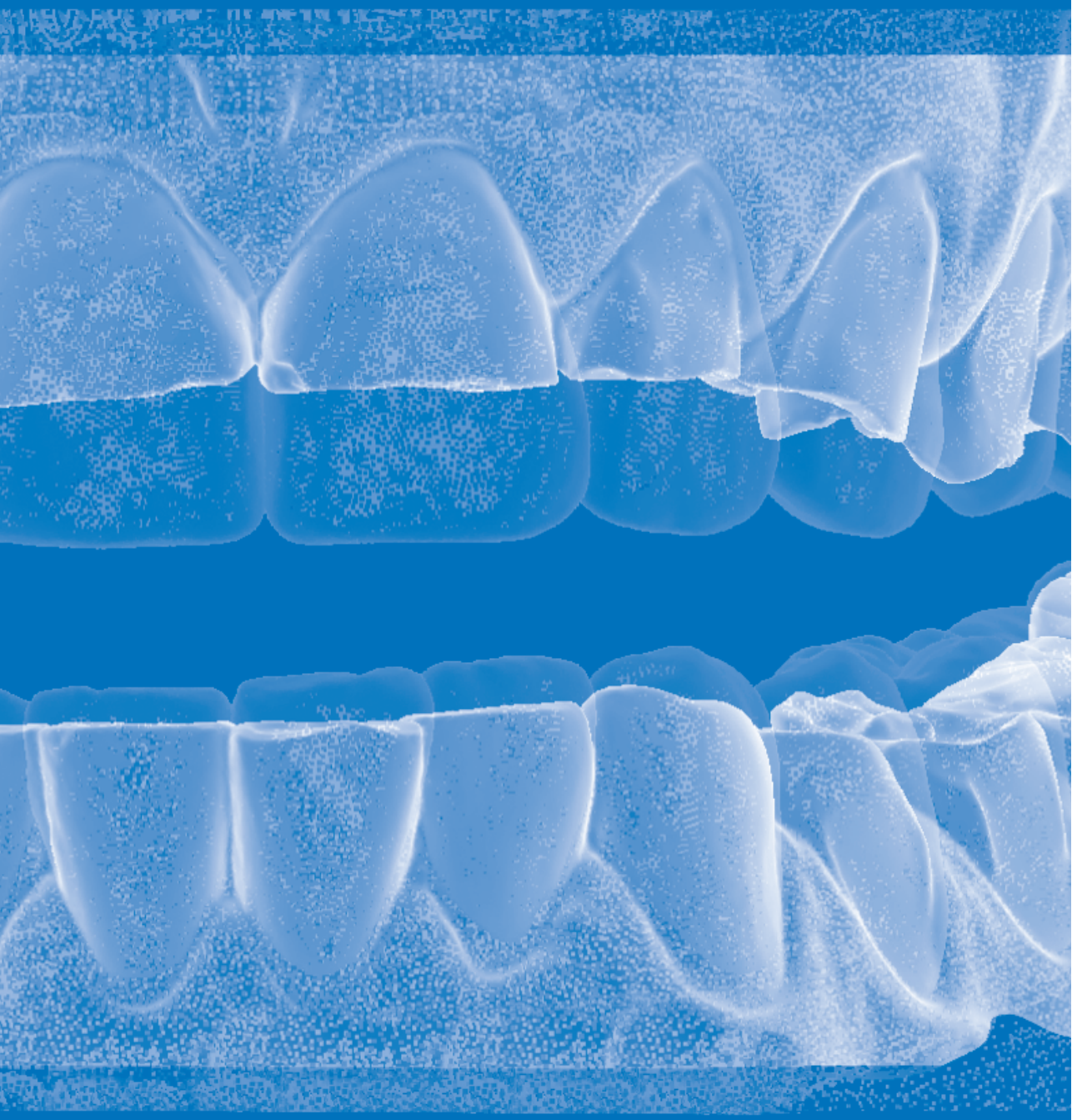

1

GENERAL INTRODUCTION

1 INTRODUCTION

Teeth are frequently exposed to erosive, abrasive, and attritive factors. This culminates in the progressive wear of the mineralized tissues. This phenomenon is age-related and the degree of tooth wear that is proportionate to the patient's age is described as 'physiological tooth wear' [1,2]. In younger patients, one can expect a lower degree of tooth wear compared with patients in the later stages of their lives. Tooth wear has been described to be the third most frequently observed dental condition (after dental caries and periodontal disease). The prevalence of tooth wear with dentin exposure (Fig 1) in younger patients has been estimated at 20% to 45% for permanent teeth, and it has been suggested that its prevalence is increasing in the Dutch population [3,4].

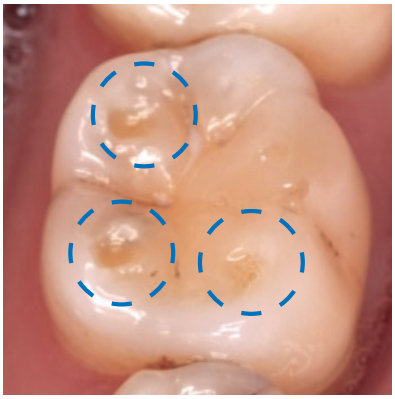

Figure 1: Molar tooth with dentine exposure due to tooth wear

When the degree of presenting tooth wear exceeds the physiological levels of wear that would be expected for age, it is regarded as 'pathological tooth wear' [1]. The terms 'physiological' and 'pathological' wear refer to the levels of tooth tissue loss relating to the patient's age, however, they do not describe the amount of tooth substance lost. The term 'severe tooth wear' is used to describe the extent of the tooth wear when 1/3, or more, of the clinical crown is lost[1]. Both pathological and severe tooth wear may cause pain or discomfort, functional problems, or deterioration of aesthetic appearance, which, if it progresses, may give rise to undesirable complications of increasing complexity, and may have adverse effects on the oral health-related quality of life.

Tooth wear is related to lifestyle and has a multifactorial etiology[1,5]. When preparing a personalized care plan, it is important to identify the etiological factors e.g., dietary habits, gastro-oesophageal reflux, and parafunctional habits. Attributing the

(single) dominant etiological factor of tooth wear at an individual level is difficult, as multiple factors (often) interplay. The traditional approach is to differentiate the etiological field into three categories i.e., abrasion, attrition, and erosion[6]. Attrition has a mechanical origin, with tooth-tooth contact because of physiological function, or parafunction. The latter includes habits of tooth grinding and tooth clenching. Abrasion is the mechanical wearing-away of teeth due to interaction with objects other than tooth-tooth contact e.g., nail-biting, oral hygiene routines, or the interaction with (abrasive) substances e.g., consumption of sunflower seeds. Erosion is described as the chemical dissolution of tooth substance without the presence of plaque. The acids responsible for erosive tooth wear are not products of the intraoral flora but stem from dietary, occupational, or intrinsic sources. Frequent contact between acids and a tooth's surface can cause erosive tooth wear.
The modern approach when preparing a personalized care plan is to focus on chemical and mechanical causes [7]. Chemical tooth wear (erosion) can be caused by intrinsic factors (acidic content of the stomach) or by extrinsic factors (acidic diet). Mechanical tooth wear can also be extrinsic and intrinsic. Extrinsic factors include the chewing of abrasive food components and the use of highly abrasive dental care products which cause abrasion. Intrinsic factors include habits of tooth clenching and tooth grinding, which lead to attrition.

2 CLINICAL MANAGEMENT OF TOOTH WEAR

The presentation of tooth wear is diverse, as patients may present themselves at different stages of tooth wear, with differing patterns, and with different etiological factors. Patients may seek dental care when their tooth wear results in symptoms of sensitivity and/or pain, difficulties chewing and eating, impaired orofacial aesthetics because of loss of dental tissue, and 'crumbling' of dental hard tissue and restorations, threatening the integrity of teeth. Alternatively, the patient may simply be worried about the condition and life expectancy of their dentition[1,8,9]. When the tooth wear is in its more advanced stages, or when the level of wear is in its early stages and progressing rapidly, patients may report these symptoms. In these cases, tooth wear can have an adverse effect on the oral health-related quality of life (OHRQoL)[10-13]. Advanced stages of tooth wear may also risk the integrity and prognosis of a patient's dentition, further limiting their OHRQoL.

Figure 2 is a flow chart illustrating a recently proposed decision-making process for a patient with tooth wear[1]. In patients with physiological tooth wear, no treatment is needed. In patients with pathological tooth wear, when symptoms mentioned above are observed, additional care is required. The first step in any dental care plan is

risk assessment. Risk assessment is an important aspect of evidence-based, patient-centered decision-making in modern healthcare. In tooth wear patients, it includes diagnosis of the etiology and documentation of the amount of wear [8]. With an accurate diagnosis of the etiology, etiology-specific advice can be given to patients, to prevent further progression of their tooth wear (counselling). As part of the monitoring process to ensure the efficacy of the counselling provided, tooth wear progression may be appraised using a variety of tools including (but not limited to) the use of serial dental casts or digital 3D scans. These tools may also be used to improve the patient's awareness of the disease and to explain the nature and severity of the presenting condition. This contributes to the patient taking ownership of their problem, which is a key factor in effective clinical management. Monitoring can also provide additional information to help identify the etiology of the presenting tooth wear. 'Counselling and monitoring' is the second step of the clinical management of tooth wear.

When the tooth wear results in limited problems, counselling and monitoring may suffice irrespective of the stage/ severity of the condition[1,8,14]. When there is a clear demand for restorative treatment by the patient, or when there is a cause for concern for the clinician, restorative treatment may be necessary.

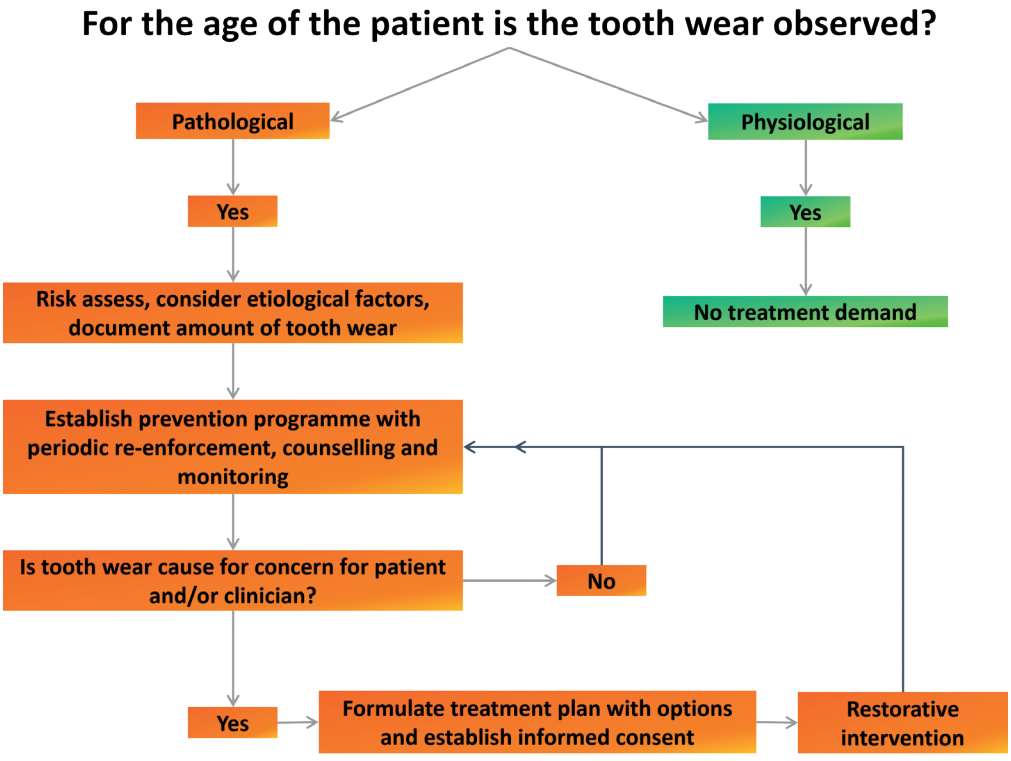

Figure 2: Flow chart: Decision-making process of a patient with tooth wear [1]

3 RESTORATIVE TREATMENT OF TOOTH WEAR

The goal of restorative treatment of tooth wear is to apply restorative material to the worn tooth surfaces with the aim of compensating for the lost tooth substrate and simultaneously attaining an aesthetically pleasing outcome. These restorations may be regarded as a form of protective layer for the dental hard tissues and for the pulpal tissues. This form of intervention also has the potential to improve oral function. Thus, restorative treatment should contribute to an overall enhancement of the patient's well-being and their OHRQoL. The recognition of patients' quality of life and well-being as pivotal outcomes in medical research is increasingly gaining prominence.

In patients with tooth wear, minimally invasive approaches should be preferred over invasive approaches such as traditional indirect restorations, which require extensive preparations, sacrificing sound tooth tissue [1,8,14]. Thus, restorative intervention where possible should be provided "additively". A direct consequence for additive restorative treatment of tooth wear is the introduction of a planned increase in the vertical dimension of the occlusion – 'VDO-increase.' This can be 3 mm or more, to create sufficient inter-occlusal space for the placement of the desired restorative material at the molar areas. A clinical parameter relating to the VDO is the freeway space (FWS). The FWS is the space between the occluding surfaces of maxillary and mandibular teeth when the mandible is at rest, also known as the clinical resting position (CRP)[15]. Generally, the FWS of dentate patients is within the range of 2-4 mm. To optimally restore worn-down teeth, there is the need to plan an increase in the VDO which can be equivalent to or greater than the pre-treatment CRP, thereby possibly hampering the patient's ability to adapt to the new situation[16,17]. This can introduce functional problems such as pain and discomfort at the temporomandibular joints and the associated musculature, alterations in speech, and increased muscle activity. These symptoms can also impair the patient's OHRQoL. Also, higher occlusal loads that can be applied because of the increased VDO are associated with raised failure rates of restorations, especially in the short term[18]. Some authors have advocated approaches that enable a reversible verification of the planned VDO-increase, before definitive restorative rehabilitation as a necessary step when planning these complex rehabilitations[19,20]. However, presently there is the absence of a randomized clinical trial directly comparing the outcomes of treatment with and without a prior evaluation of the VDO-increase.

Generally, conservative dental procedures can include the application of either directly (chairside) fabricated, or indirectly (extra-orally) constructed restorations. The direct application of resin composite restorations is one of the treatment

options commonly prescribed for the treatment of tooth wear. This approach offers the merits of relatively low treatment cost, as well as the ease of repair and adjustment in the event of (partial) restoration failure. However, a key disadvantage of this treatment modality is the need for appropriate operator technical skill and knowledge to help acquire optimal anatomical restoration form, while introducing the required increase in the VDO. The use of indirect techniques may, however, allow optimal restorations to be attained more readily when compared to the direct approach. Furthermore, the desired VDO-increase can also be planned extra-orally, further facilitating operators. The fabrication process of indirect restorations can either be performed conventionally 'by hand' by a dental technician using stone cast (die) models or performed using modern CAD/CAM fabrication techniques. However, the indirect technique for restoration manufacture is associated with higher treatment costs.

4 THE LONGEVITY OF RESTORATIVE TREATMENT OF TOOTH WEAR

The restorative treatment of tooth wear in itself does not remove the factors which have contributed to the tooth wear. These etiological factors pose a risk to the longevity of restorations. Habits of tooth clenching and tooth grinding result in early restoration fracture[21]. Erosion and/or habits of tooth clenching and tooth grinding cause progressive wear, resulting in the need for new restorations. This accelerates the restorative cycle and patients with tooth wear can be regarded as 'high-risk patients.' Therefore, clinical data relating to the longevity of restorations (e.g. class II restorations[22], single unit indirect restorations[23]) amongst regular (non-tooth wear) patients is not as applicable whilst attempting to determine the optimal type of dental material or fabrication technique when restoratively treating tooth wear.

Clinical data on the longevity of restorations in the restorative treatment of tooth wear is limited. The commonly applied outcome measure when reporting on the survival of dental restorations is the Annual Failure Rate (AFR). The AFR describes the percentage of restorations that fail per annum. A systematic review, evaluating 12 studies, reported considerable variations in the longevity of direct and indirect restorations placed for the treatment of tooth wear[24]. For direct composite restorations, AFRs ranged from 0.7% (excellent) to 26.3% (unacceptable) amongst these patients, illustrating the large variation between the studies. Only three studies in this systematic review evaluated indirect restorations. Indirect restorations had AFRs ranging from 0% (excellent) to 14.9% (unacceptable). Within the literature,

comparative studies involving the use of direct and indirect application techniques for the restorative treatment of tooth wear, are lacking. Furthermore, studies on the longevity of novel CAD/CAM restorations in these patients are scarce.

Depending on their size, modern resin composites can be divided into micro-filled, nano-filled, and hybrid-filled composites, with the latter constituting a combination of filler sizes [25]. In regular (non-tooth wear) patients, long-term clinical performance is not affected by the subtype of composite, with acceptable outcomes for both hybrid, micro-filled, and nano-filled composites [22], however, inferior outcomes have been reported with the use of micro-filled composite restorations when placed at loadbearing areas for the treatment of tooth wear [26]. Micro-hybrid composites have shown good clinical performance in patients with tooth wear [24,27], but no data on nano-filled composites in patients with tooth wear is available.

5 RADBOUD TOOTH WEAR PROJECT

Data for the thesis originates from the Radboud Tooth Wear Project (RTWP)[14]. The RTWP commenced in 2010 at the Department of Dentistry, Radboud university medical center (Radboudumc), Nijmegen, The Netherlands. It is a clinical project, focusing on the clinical management of worn dentitions, including counselling and monitoring and the use of minimally invasive restorative treatment approaches amongst patients with diverse levels of dental comorbidity. Patients are referred to the RTWP by their general dental practitioners for the assessment and treatment of their worn dentition. Multiple trials are embedded within the RTWP.

Patients meeting the eligibility criteria were included in the embedded studies of the RTWP (Fig 3). When these criteria were met, baseline registrations were performed. This includes a clinical assessment of the levels of presenting tooth wear, as well as the taking of baseline dental impressions, intra-oral 3D scans, intra-oral photographs, and the use of questionnaires to assess their OHRQoL.

In cases without functional or aesthetical demands and with no patient-based request for restorative care, no restorative treatment was prescribed, regardless of the level of tooth wear. These patients were included in one of the embedded studies: Counselling and Monitoring. Progression of tooth wear and its consequence on the OHRQoL were studied in a prospective design. Other study arms of the RTWP included patients, where the need for restorative treatment was jointly decided between the dentist and the patients, as part of a 'shared decision-making' process. Where restorative treatment was agreed upon, patients were assigned to a dentist

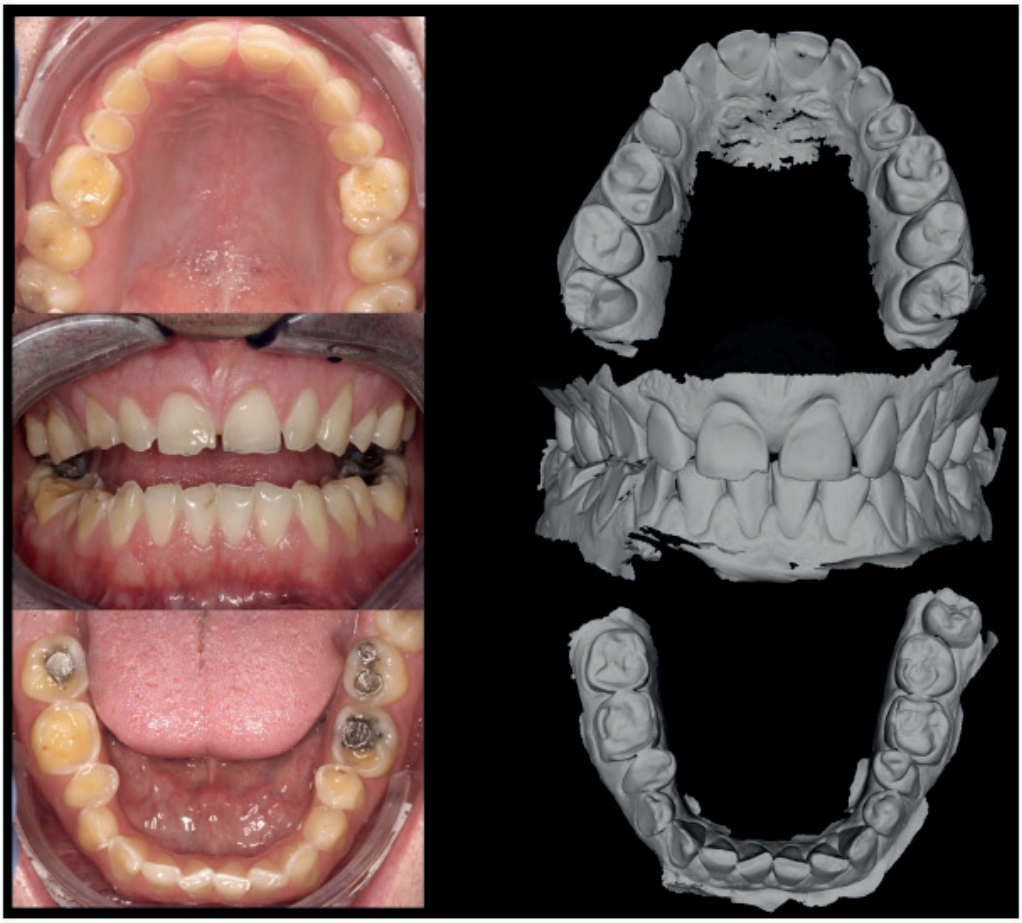

Figure 3: An example of a patient with severe tooth wear. Patient from one of the trials embedded in the RTWP

who is well-trained in the restorative procedure, and were assigned to one of the restorative study arms. These prospective studies evaluated different restorative treatment protocols and are independent clinical trials.

The protocol for direct composite restoration starts with the restoration of the mandibular anterior teeth, followed by maxillary anterior teeth. Subsequently, mandibular posterior teeth are reconstructed, and the protocol is completed with the restoration of the maxillary posterior teeth. The planned VDO-increase is determined extra-orally and this information is transferred intra-orally with the aid of silicon stops. To ensure optimal shaping and occlusal contacts at the load-bearing

surfaces of teeth, the operators used the application technique of direct shaping by occlusion (DSO)[28]. Direct veneer restorations are applied at the facial surfaces of teeth to improve the aesthetic appeal. The protocol for indirect restorations (sometimes in combination with directly applied restorations), consists of additive occlusal 'tabletop' restorations at (pre)molar teeth, and additive palatal/lingual veneer restorations at the anterior teeth, thereby helping to ensure a minimally invasive treatment approach.

The independent clinical trials were designed to evaluate specific aspects of the restorative treatment protocols as well as the beneficial effects of the outcomes from the perspective of patients and dental professionals. Outcomes from the perspective of patients included changes to their OHRQoL and the need for interventions to (failed) restorations. Outcomes from the perspective of dental professionals included the longevity of restorations and the effect of specific variables on it. The studies in the RTWP aimed to evaluate the effect of the material, the application technique, the increment of VDO, and the etiology of tooth wear on the longevity of restorations and patients' dentitions.

6 AIM AND OUTLINE OF THE THESIS

This thesis will focus on outcomes from the perspective of both patients and operators and it will assess the relevance of specific factors involved in treatment success of restorative treatment of tooth wear based on (mainly) clinical studies.

The questions to be answered in this thesis are:

- Is the reversible tryout of the VDO-increase prior to restorative treatment of tooth wear a necessary step in the restorative treatment plan?
- Do directly and indirectly applied resin composite restorations for the restorative treatment of generalized tooth wear have different clinical performance outcomes?
- How can a worn dentition be restoratively treated using a digital workflow?
- What is the clinical performance of CAD/CAM (indirect) nanoceramic restorations in tooth wear patients, after 1 year?
- Do different resin composite materials have a similar (susceptibility to) mechanical degradation *in vitro*?

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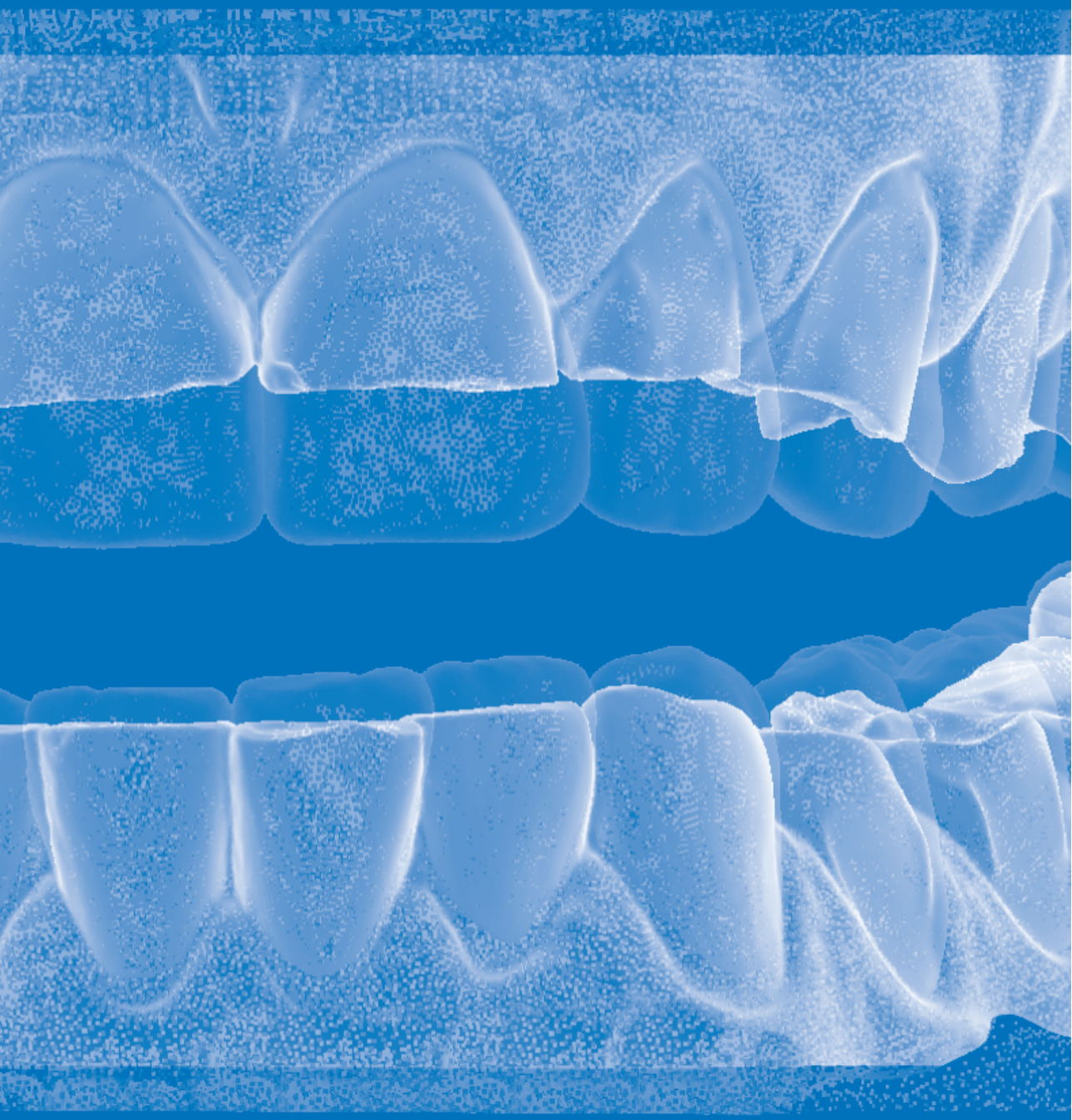

2

RANDOMIZED CONTROLLED TRIAL ON TESTING AN INCREASED VERTICAL DIMENSION OF OCCLUSION PRIOR TO RESTORATIVE TREATMENT OF TOOTH WEAR

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ABSTRACT

Background: Evaluation of a new vertical dimension of occlusion (VDO) in complex restorative treatments is considered a necessary step prior to placement of restorations.

Objectives: This Randomized Controlled Trial (RCT) aimed to assess the effects of using an evaluation of a VDO-increase before restorative treatment in patients with moderate to severe tooth wear, on OHRQoL, freeway space (FWS), and interventions to restorations.

Methods: Forty-two patients with tooth wear were included and randomly allocated to either a test phase with a Removable Appliance (RA) or no test phase. Restorative treatment consisted of restoration of all teeth using composite restorations in an increased VDO. OHIP-score, freeway space (FWS), and clinical acceptability of restorations were assessed at baseline and at recall appointments (1 month and 1 year). Intervention to restoration was scored in case of material chipping or when the abutment tooth had increased sensitivity that could be linked to occlusal overloading. ANCOVA analyses, Univariate Cox regression, t-Tests, and descriptive analyses were performed ($p<0.05$).

Results: Clinical follow-up after 1 year was completed for 41 patients. No significant effect of testing the VDO with a RA could be found on the OHIP-score ($p=0.14$). Reduction of FWS in the RA group, compared to the control group, was significantly lower at 1 year ($p=0.01$, 95%CI -1.09 to -0.15). No effect on early interventions to restorations was found ($p=0.94$).

Conclusion: This RCT showed that a removable appliance is not indicated to functionally test the increased VDO prior to restorative treatment in patients with tooth wear.

1 INTRODUCTION

One of the controversial issues in restorative dentistry is increasing the Vertical Dimension of Occlusion (VDO). The VDO is the distance between two selected anatomic or marked points (usually one on the tip of the nose and the other on the chin) when in maximal intercuspal position.[1] Traditionally, VDO was assumed to be constant throughout an individual's life.[2] As a result, a VDO-increase was thought to interfere with the physiology of the neuromuscular complex. It was thought to result in symptoms of function-related problems[3-5] such as pain in the Temporo Mandibular Joint (TMJ),[2,4] affected speech,[2-4] and increased muscle activity potentially causing higher occlusal loading and an increased failure rate of restorations.[6] Modern perspectives consider the stomatognathic system to be more dynamic in nature, including a comfortable VDO that occurs in a range. Changing the VDO then initiates an adaptive process that may or may not be associated with some of the symptoms mentioned before.

Certain dental procedures require a VDO-increase in dentate patients, such as the restorative treatment of tooth wear. Tooth wear is a physiological process resulting in loss of natural tooth tissue over time.[7] In some patients tooth wear can become pathological. Pathological tooth wear relates to active wear of atypical rate and nature[7]. It compromises the prognosis of the dentition[7] and can result in reduced Oral Health-Related Quality of Life (OHRQoL),[8] due to aesthetical and functional problems.[7,8] The clinical management of severe tooth wear usually includes restorative treatment, preferably in a minimally invasive approach. It involves additive application of restorative material to occlusal and incisal surfaces,[7] and by definition this will result in a VDO-increase.
A parameter closely related to the VDO is the freeway space (FWS). This is the space between occluding surfaces of the maxillary and mandibular teeth when the mandible is at rest (Clinical Resting Position; CRP).[1] It is generally accepted that the FWS occurs within the range of 2-4 mm. As the TMJ opens by rotation first, distance of 4 mm in the anterior region corresponds with a distance of 2 to 3 mm in the posterior region[9]. To provide sufficient space for restorative material in the posterior area in a severe tooth wear patient, the VDO-increase could be 3 mm or more in the molar region, consequently increasing the VDO up to or beyond the clinical resting position. In such a case, the risk of functional problems is expected to be higher as patients have to acquire a new CRP.[6,10]

A reversible try out of the new VDO has been regarded as a necessary step before complex rehabilitations.[11,12] This evaluation focuses on maladaptation and functional problems that might necessitate the dentist to change or even abandon the planned

restorative rehabilitation, thus preventing situations where expensive restorations must be adjusted or removed. Transparent polymethylmethacrylate Removable Appliances (RAs) are commonly used, inserted in one arch, in which the entire change of VDO is represented. Such RAs have low costs but they themselves are associated with aesthetic and functional disadvantages and may challenge patients' compliance.[5] Acrylic resin splints, temporarily cemented in the lower jaw, have also been used but patients' discomfort up to 2 months has also been reported.[6,10,13,14]

In some studies on restorative rehabilitation of generalized tooth wear in patients without (a history of) Temporo Mandibular Dysfunction (TMD) 'definitive' restorations were placed without prior testing of the increased VDO.[15,16] No observations of maladaptation or substantial functional problems needing further care were reported, although speech difficulties could be observed in the first weeks.[17] Studies on restorative rehabilitation of localized tooth wear without prior testing of the VDO-increase also did not report function-related problems, except for temporary speech difficulties.[18] In addition, no occlusal overloading causing sensitivity of the abutment teeth was reported. These results are also reflected in a systematic review,[5] stating that increments of VDO up to 5 mm can be safely introduced without prior testing, although it remains unclear if the increment was considered at the incisal pin of a dental articulator or the molar region.

Notwithstanding these reports, as there is no randomized controlled study directly comparing the outcomes of treatment with and without prior evaluation of the VDO-increase, there is a need for more evidence. This randomized controlled trial aimed to assess the effects of using an evaluation of a VDO-increase using an acrylic RA before restorative treatment in patients with moderate to severe tooth wear on 1) OHRQoL, 2) FWS, and 3) the need for early interventions to restorations on sensitive abutment teeth due to occlusal overloading or to restorations with early failures.

2 MATERIALS AND METHODS

Study design

This study was a single-center, Randomized Controlled Trial (RCT). it was designed and conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Its design and protocol were approved by the local ethics committee (CMO Arnhem-Nijmegen file nr. NL31371.091.10), prior to commencement. After completion of the study, it was registered on ClinicalTrials.gov (NCT04797494). Sample size calculation was based on a parallel randomized trial, evaluating directly and indirectly applied composite restorations when used as palatal veneer

restorations to maxillary anterior teeth and when used as 'tabletop' restorations on first molars. [19]. It assumed a 15% difference in survival of restorations resulting in a group size of 75. An interim analysis showed that the failure rate of indirectly placed restorations was considerable and already reached statistical significance. It was then decided to stop inclusion. No differences could be observed when evaluating direct and indirectly placed restorations when used as palatal veneer restorations to maxillary anterior teeth. Indirectly placed 'tabletop' restorations showed inferior survival rates compared to the directly applied composite restorations on first molars with a hazard ratio of 3.4. It was concluded that the indirect composite was not suitable for molar restorations when used in severe tooth wear patients.

Inclusion and randomization

General dental practitioners referred patients to the Radboud Tooth Wear Project at the Department of Dentistry of the Radboud university medical center (Nijmegen, The Netherlands). Patients' eligibility was briefly assessed based on inclusion and exclusion criteria. The inclusion criteria were: (1) age > 18 years; (2) generalized moderate to severe tooth wear, (TWI [20] ≥ 2) ; (3) a patient's demand for treatment; (4) full dental arches except for 1 missing (pre)molar in the posterior area; (5) minimal estimated required VDO-increase for first molars of ≥ 3 mm. The exclusion criteria were: (1) limited mouth opening or (history of) TMD; (2) advanced periodontitis, deep caries lesions, or multiple large restorations including multiple teeth with endodontic problems; (3) local or systemic conditions contra-indicating dental procedures. Parafunctional habits of grinding or clenching and gastroesophageal reflux disease were not considered exclusion criteria.

A random allocation sequence of treatments was digitally generated by a statistician (EB). No stratification for VDO-increase was performed. Block randomization was used with a block size of eight. The sequence was generated with an intended ratio of 1:1 and was handled with sealed envelopes. Patients were included after providing written informed consent and allocated to either testing the VDO-increase prior to restorative treatment (test group) or allocated to not testing the VDO-increase (control group).

Patients were assigned to one of 7 operators, aiming for an even distribution of patients among operators, who were staff members of the Department of Dentistry of the Radboud university medical center. Prior to the onset of the study, they participated in multiple calibration sessions for the clinical procedures of this trial. Definite determination of matching inclusion and exclusion criteria was done based on specific clinical data: i.e., intra-oral examination, digital photographs, full-arch stone cast models, bitewing radiographs, and when indicated, a panoramic

radiograph. Some previously included patients had to be excluded.

Clinical procedures

Two operators (NO and CK) made a consensus estimate of the VDO-increase needed for restorative rehabilitation. The increase was determined by assessing cast models, mounted in an articulator, for the height loss of teeth with the largest amount of wear, related to the original anatomic form of teeth. In addition, FWS and aesthetic limits of lengthening the anterior teeth were considered. The estimated required VDO-increase was measured at the articulator's pin.

Patients allocated to the test group received an acrylic full-arch RA (Figure 1). The desired VDO-increase for the restorative rehabilitation was represented in a single RA. The RA was made using the cast models, mounted in an articulator by a dental technician. Generally, the RA was made for the mandible and it was designed to evenly distribute occlusal contacts. Patients were instructed to wear the RA 24 hours per day for a period of 3 weeks, except when cleaning the dentition. After testing, restorative treatment commenced. Patients allocated to the control group received no RA.

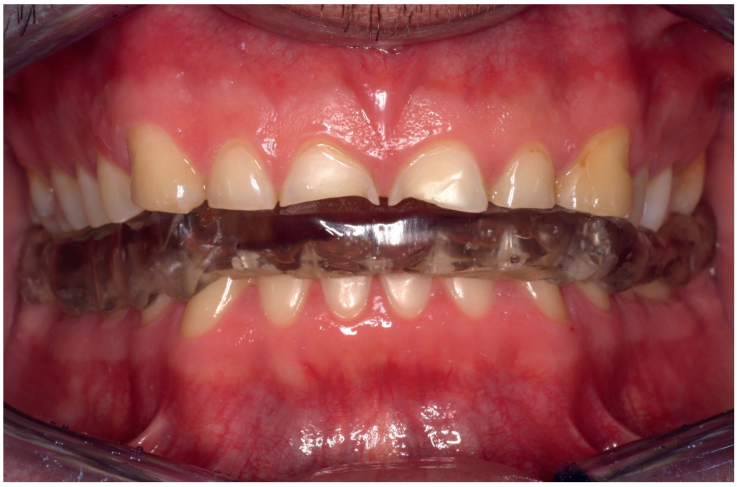

Figure 1: Example of acrylic removable appliance placed on mandibular teeth

Figure 2 shows the initial situation of one of the patients. Restorative treatment consisted of restoration of all teeth, individually, using composite restorations in the desired new VDO. Wisdom teeth were refrained from restorative treatment. Restorations were placed either directly or indirectly as part of a parallel randomized group trial.[19] Regardless of the technique, it was aimed to achieve

a balanced occlusal relationship. Where necessary, occlusal adjustments were made immediately after restoration. Figure 3 shows the situation after restorative treatment

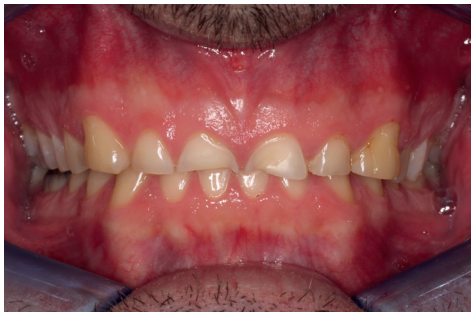

Figure 2: Initial situation

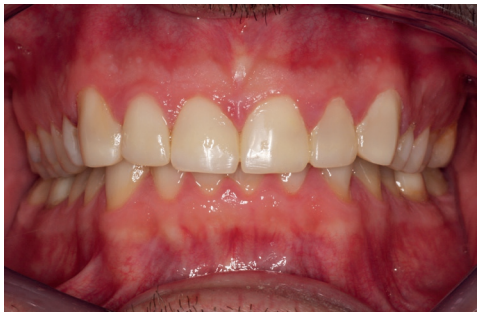

Figure 3 : Situation after restorative treatment

Recall appointments were scheduled for 1 month and 1 year after completion of restorative treatment. The dentition was evaluated and documented by intra-oral examination, intra-oral digital photographs, and digital 3D scans (LAVA COS/ TrueDef, 3M). Participants could not be blinded for the treatment with or without a RA. Neither could the operator that performed the restorative procedure. Care providers that performed the follow-up examinations were blinded.

Measurement Outcomes

Patients completed the OHIP-46 questionnaire at baseline and the recall appointments. The original OHIP questionnaire consists of 49 statements.[21] Three statements (no. 9, 18, 30) were deemed not applicable as they addressed full dentures and were omitted. Patients were asked how often they experienced the impact of each statement. Answers were scored on a 5-point ordinal scale, ranging from never (1), hardly ever (2), occasionally (3), and fairly often (4), to very often (5). Higher scores imply a more impaired OHRQoL.

FWS was measured prior to restorative treatment, to help establish the increment of VDO, and at the recall appointments. Patients were in sitting upright and they were instructed to count backward from 70 to 60. Then, patients received supportive instructions as to how to relax the mandibular muscles. Meanwhile, a plastic, non-digital millimeter ruler was placed in front of the anterior teeth to evaluate the intermaxillary space.[22]

Patients allocated to the test group completed an additional questionnaire of 43 statements immediately after having worn the RA for 3 weeks. This questionnaire

is a derivate of the OHIP questionnaire.[21] The questionnaire specifically addressed functional abilities, functional problems, and the level of comfort of the RA. Answers were scored on a 5-point ordinal scale, ranging from never (1), hardly ever (2), occasionally (3), and fairly often (4), to very often (5). In addition, patients were asked about their compliance. Patients scored the time they actually wore the RA, divided into 4 categories: (1) 20-24h, (2) 12-20h, (3) 5-12h, and (4) <5h per day.

Restorations were assessed at the level of clinical acceptability, focusing on fractures and material chippings at both recall appointments. Failure was defined as restorations that either needed to be (1) replaced, when severe deficiencies were observed i.e., extensive or multiple fractures or in case of loss of the tooth, (2) repaired, when localized deficiencies were observed i.e., adhesive fractures, (3) refurbished by polishing, when the restoration showed a small material chipping. Additionally, patients were asked to report sensitivity of abutment teeth that might be linked to occlusal overloading and those restorations received occlusal adjustment.

Acquired 3D scans (of cast models) at baseline and recall after 1 month were evaluated in a software program (MeshLab v2021.07). The distance between the deepest point on the buccal gingival border of the first molar in the upper jaw and that of the lower jaw was measured on the right and left sides, separately. Mean scores were calculated and regarded as the realized VDO-increase, according to the procedure described by Mehta et al.[15]

Statistical analyses

The effect of the RA on OHRQoL and FWS was analyzed by performing an ANCOVA analysis in which both the baseline score and the allotted treatment were regarded as a variate. The ordinal data of the OHIP questionnaire was handled as metric data.

To evaluate the effect of the treatment as a whole, OHIP mean scores and FWS scores were analyzed with paired student t-Tests for each group separately, comparing baseline scores with scores after 1 month and after 1 year, separately.

Descriptive analyses were performed for the questionnaire addressing the RA.

The effect of the RA on early failure rate of restorations after 1 year was analyzed using a univariate Cox model, using a shared frailty term to adjust for the dependency of data, as multiple restorations were clustered within one patient. Descriptive analysis was conducted for the failure rate of restorations after 1 month.

The analyses were conducted within the R-software (v 3.6.2) and SPSS-software (v 25). The significance level was set for all tests at $p<0.05$.

3 RESULTS

Patients were included and assigned to the specific intervention between February 2011 and October 2014 by a researcher not involved in the treatment (BL). Restorative treatment was conducted between October 2011 and July 2015. Follow-up was completed between November 2011 and April 2017. An interim analysis was performed on the parallel-group trial, evaluating the survival of two treatment techniques, and showed a considerable difference that reached a statistical significance. Therefore, inclusion was stopped earlier than anticipated. Continuing the study inclusion was not deemed ethical.

Randomization resulted in an allocation of 25 patients to RA and 24 patients to no-RA. After definite determination of matching inclusion and exclusion criteria, 4 patients allocated to RA had to be excluded (1x multiple missing posterior teeth, 3x VDO-increase<3mm) and 3 patients allocated to no-RA had to be excluded (1x multiple missing posterior teeth, 1x deep caries lesions, 1x VDO-increase<3mm). This resulted in, 42 patients (36 males, 6 females) included in this RCT. Clinical follow-up was completed for 41 patients. No unintended effects were observed during the study. One (female) patient, allocated to the no-RA was lost to follow-up for personal financial reasons. Two patients allocated to the no-RA could not be recalled after 1 month for personal reasons, although they were recalled after 1 year. The flow chart of the clinical study is shown in Figure 4.

Statistical analysis was conducted for 41 patients; 21 patients (2 female) allocated to RA (mean age: 37.1 ± 6.1 y), and 20 patients (3 female) allocated to No-RA (mean age: 36.6 ± 6.5 y). The mean observation time at recall 1 month, including censoring, was 2.0 ± 1.0 months (range: 0.7-6.4). The mean observation time at recall 1 year was 15.2 ± 3.4 months (range: 9.8-24.0). Due to personal reasons, 1 patient allocated to RA, actually did not receive the RA. Statistical analysis was performed according to the Intention-To-Treat principle.

After 3 weeks of having worn the RA, none of the patients allocated to the RA reported symptoms of function-related problems that otherwise would have required a change of the planned restorative treatment. After restorative treatment, none of the patients in both groups reported symptoms of maladaptation. The mean realized VDO-increase measured at first molars, was 2.3 mm (± 0.6) in the RA-group and 2.2 mm (± 0.6) in the no-RA-group.

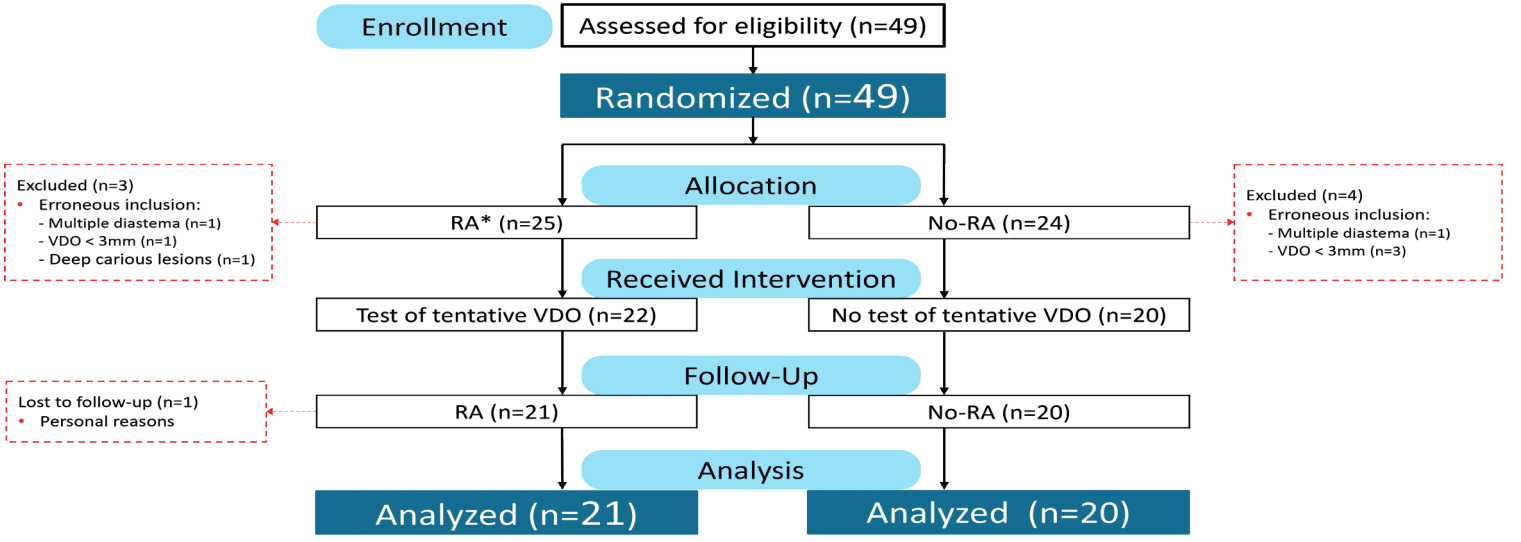

Figure 4: Flowchart of the handling of patients regarding allotted treatment, follow-up and analysis. *One patient allocated to the RA-group received the No-RA-group treatment for personal reasons. Analyses were performed conform the Intention-to-Treat principle

The treatment as a whole, including restorative treatment, showed a significantly positive effect on the OHRQoL after 1 month ($p<0.03$) and after 1 year ($p<0.001$), regardless of the experimental group (for statistical analysis see the supplementary table. Calculated Cohen's D effects sizes were -2.78 and -1.56 after 1 month and -1.88 to -1.62 after 1 year, indicating a large effect of the treatment as a whole on the OHRQoL. Results for OHRQoL-changes for RA and No-RA after 1 month and 1 year are visualized in Figure 5. It shows the considerable variation in changes, with similar outcomes for both groups. No significant effect of testing the VDO-increase with a RA could be found in the ANCOVA analysis, that corrects for the baseline situation, on the OHRQoL after 1 month (p=0.14, 95%CI -0.05 – 0.19), nor after 1 year (p=0.76, 95%CI: -0.14 - 0.19) (Table 1).

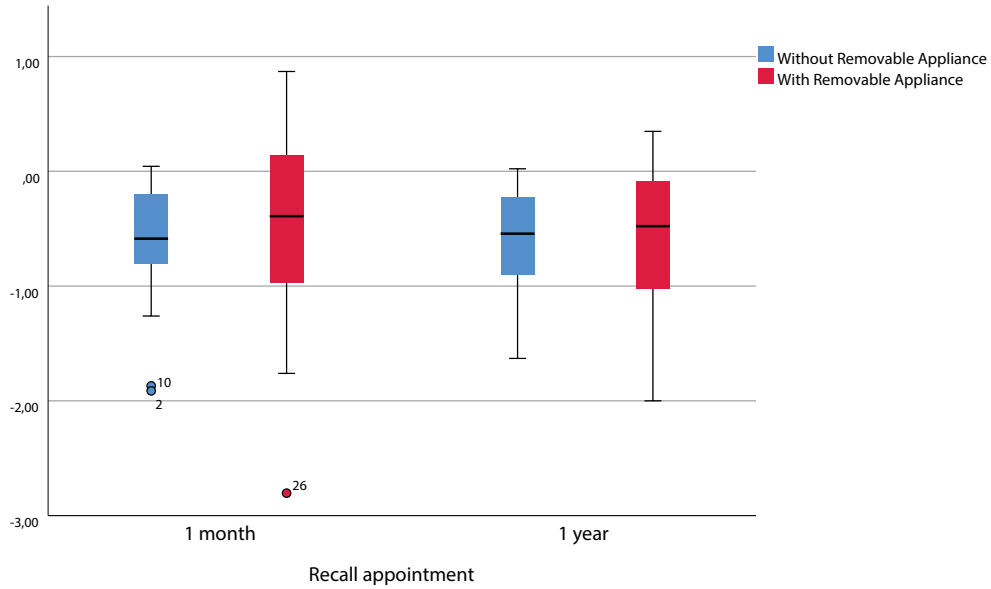

Figure 5: Change in mean OHIP-score (Baseline to recall). Positive values indicate improvement.

The treatment had a significant effect on FWS after 1 month ($p<0.007$) and after 1 year ($p<0.002$), regardless of the experimental group: with reduced FWS at both 1 month (RA 1.2 mm; no-RA 1.4 mm) and 1 year (RA 1.1 mm; no-RA 1.7 mm) (see Table 4 online material).

No significant effect of testing the VDO with a RA on the FWS reduction after 1 month could be found in the ANCOVA analysis (p=0.69, 95%CI -0.79 – 0.53). However, ANCOVA analysis showed that FWS reduction in the RA group was significantly lower after 1 year (p=0.01, 95%CI -1.09 to -0.15) (Table 1).

Twenty out of 21 patients allocated to the RA-group completed the questionnaire addressing the RA. Patients frequently reported difficulties when chewing, troubles with pronouncing, unclear speech, sore jaw, sore spots, and discomfort about their appearance when wearing the RA (Table 2). Eight participants reported having worn the RA for 20-24h per day. Five patients reported 12-20h, 3 patients reported 5-12h, and 4 patients reported less than 5 hours per day.

In this group of patients, 1,660 restorations were placed, with 862 restorations placed in the RA-group and 798 restorations placed in the no-RA-group. The average number of restorations per patient was 41 (± 5). After 1 month, 1 restoration in the test group received occlusal adjustment after the patient reported sensitivity of the abutment tooth and requested modification. At recall 1 month, 8 failures were observed of which 5 restorations failed in the test group and 3 restorations failed in the control group (table 3). At recall 1 year, 59 failures were observed, of which 36 restorations failed in the test group and 23 restorations failed in the control group (table 3). Fracture was the main failure modality. No significant differences were observed comparing the allotted treatments on number of failures (p=0.94).

Table 1 Effect of allocation of treatment, corrected for the measurement at baseline

ANCOVA			Beta	95% CI of Beta	P-Value (2-tailed)
OHIP-questionnaire	Recall 1 month	Allocation	0.136	-0.05 – 0.32	0.142
	(RA n=19; No-RA n=18)	Score at baseline	0.068	-0.05 – 0.19	0.261
	Recall 1 year	Allocation	0.026	-0.14 – 0.19	0.758
	(RA n=21; No-RA n=20)	Score at baseline	0.326	0.21 – 0.44	<0.001
Freeway space	Recall 1 month	Allocation	-0.128	-0.79 – 0.53	0.691
	(RA n=13; No-RA n=11)	Score at baseline	0.629	0.41 – 0.85	<0.001
	Recall 1 year	Allocation	-0.128	-1.09 – - 0.15	0.012
	(RA n=21; No-RA n=19)	score at baseline	0.690	0.54–0.84	<0.001

Table 2: questions in the questionnaire addressing the removable appliance that had the highest mean score (range 1-5)

	Mean score
Have you had difficulty chewing any foods because of problems with your removable appliance?	3.39
Have you had trouble pronouncing any words because of problems with your removable appliance?	3.30
Have you found it uncomfortable to eat any foods because of problems with your removable appliance?	3.21
Has your speech been unclear because of problems with your removable appliance?	2.85
Have you had painful aching in your mouth?	2.65
Have you had sore spots in your mouth?	2.45
Have you been self-conscious because of your removable appliance?	2.40

4 DISCUSSION

This randomized controlled trial aimed to assess the effects of using an evaluation of a VDO-increase before restorative treatment in patients with moderate to severe tooth wear, using an acrylic removable appliance, on OHRQoL, FWS, and the need for early interventions to restorations on sensitive abutment teeth due to occlusal overloading or to restorations that have early failures. No beneficial effect for the short-term intervention rate of restorations was observed. The restorative treatment resulted in a significantly improved OHRQoL in both groups and a significantly reduced FWS, but no effect of having worn the RA was observed for the OHRQoL after 1 month and 1 year, neither for the FWS after 1 month. Only a less reduced FWS after 1 year was observed after having worn the RA ($p=0.01$). The measurement error and the different number of patients with FWS measurements after 1 month and 1 year may have resulted in this finding.

Patients allocated to the RA often reported substantial symptoms after wearing the appliance (table 3). The symptoms probably contributed to low compliance, minimizing the (functional) evaluation. The reported symptoms do not necessarily reflect the VDO increase as such, but likely relate to characteristics of the appliance: poor stability and non-physiological contours, that interfere with comfort, function, and phonetics. Paired with the additional treatment time and costs of an RA, this increases the burden of using an RA.

The main objective when testing a VDO-increase is to evaluate the ability to adapt to a new VDO by acquiring a new CRP and potentially identify those patients who

show functional limitations. Another objective is to have patients adapt to the new VDO before restorative treatment, which may prevent early failures of restorations. It is likely that our patients acquired a new CRP as the mean VDO-increase of 2.2 mm at first molars (corresponding with an increase of approximately 4 mm in the anterior region) was higher than the mean FWS-reduction of roughly 1.5 mm measured at anterior teeth. In our study, none of the patients reported maladaptation after delivery of final restorations. This represents the ability of our patients to adapt to a VDO-increase of (on average) 2.2 mm at first molars, supporting the conclusions of a systematic review.[5]

The restorative treatment procedure of both groups involved restoration of anterior teeth in the first treatment session(s), while posterior teeth were restored usually some weeks later. This interval may have contributed to the similarity between the groups. In addition, this time between treatment sessions may also have contributed to the lower than anticipated increment of VDO. As a result of a temporarily anterior only occlusion, anterior teeth may have been intruded, limiting the effective VDO-increase.

This study could not find an effect of a VDO-increase try-out with RA on the outcomes of the restorative treatment of tooth wear. A major factor may be the design of the simple RAs, which provides more discomfort to patients during wearing the device, resulting in reported complaints but also a lack of compliance. As a result, and in line with the review by Abduo et al.,[5] we recommend not to apply an RA when a VDO-increase is needed for a direct or indirect rehabilitation for severe tooth wear with minimally invasive techniques.[15,23,24] However, in specific cases, extensive and expensive indirect restorative rehabilitations are performed in these type of patients. In those cases, high-end applications like CAD/CAM, tooth-colored, splints made separately for mandibular teeth and maxillary teeth, or fixed provisional tooth-bonded restorations can be used for functional evaluations as well as aesthetic evaluations.[11,25 26] These testing modalities have anatomically contoured forms that permit realistic and more comfortable clinical evaluation of the proposed VDO-increment. It can be expected that in those cases patients are more compliant to wear the device, as it improves the aesthetics rather than reducing the aesthetics. However, it is still not clear whether these extra costs are justified.

None of the patients in our study had (a history of) TMD. TMD likely is a risk factor for a poor adaptation to a new vertical dimension. In patients with both a genuine need for a VDO-increase and (a history of) TMD, it is recommended to test the VDO-increase.[11] Also in those cases, a more comfortable and aesthetically pleasing appliance may be better appreciated.

5 CONCLUSION

In this randomized controlled trial, no beneficial effect of the usage of an acrylic removable appliance to functionally test the increased VDO prior to restorative treatment in patients with generalized severe tooth wear, could be observed. The wearing of the RA itself was associated with negative OHRQoL outcomes.

6 ACKNOWLEDGEMENTS

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Table 3: Restoration failures

Failures at Recall 1 month after restorative treatment

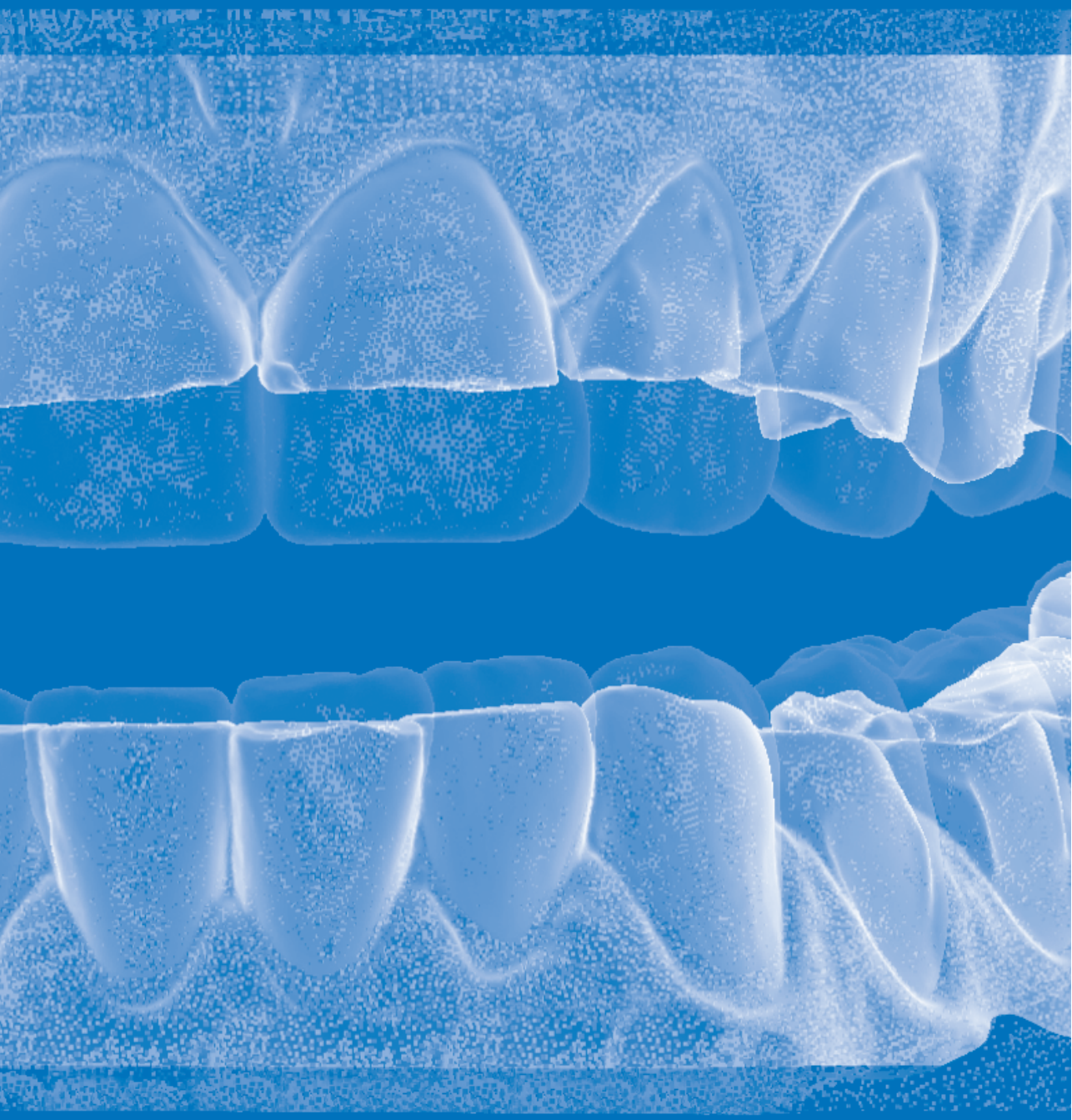
	RA-group				No-RA-group			
	Replaced	**Repaired**	**Refurbished**	**Total**	**Replaced**	**Repaired**	**Refurbished**	**Total**
Adhesive fracture	0	2	0	2	0	1	1	2
Chipfracture	0	0	2	2	0	0	1	1
Sensitivity of abutment tooth	0	0	1	1	0	0	0	
Total				5				3

Failures at Recall 1 year after restorative treatment

	RA-group				No-RA-group			
	Replaced	**Repaired**	**Refurbished**	**Total**	**Replaced**	**Repaired**	**Refurbished**	**Total**
Adhesive fracture	0	6	11	17	0	5	8	13
Chipfracture	0	3	8	11	0	3	3	6
Unknown	0	1	0	1	0	1	0	1
Wear/fracture on interface	0	0	1	1	0	3	0	3
Trauma	1	2	0	3	0	0	0	0
Complete Debond	2	0	0	2	0	0	0	0
Sensitivity of abutment tooth	0	0	1	1	0	0	0	0
Total				36				23

Supplementary table: Effect of allocated treatment (with or without Removable Appliance (RA) in combination with the restorative treatment), not corrected for the measurement at baseline

Paired Student t-Tests			*N*	*Mean (SD) Baseline*	*Mean (SD) Recall*	*Mean difference (SD)*	*Effect Size (Cohen's D)*	*95% ci of difference*	*P-value (2-tailed)*
OHIP mean score Recall 1 year	Recall 1 month	no RA + RT	18	1.94 (0.73)	1.30 (0.23)	-0.64 (0.59)	-2.78	-0.94 - -0.35	<0.001
	RA + RT	19	1.93 (0.82)	1.44 (0.32)	-0.50 (0.91)	-1.56	-0.94 - -0.06	0.029	
	no RA + RT	20	1.90 (0.72)	1.28 (0.33)	-0.62 (0.49)	-1.88	-0.85 - -0.39	<0.001	
	RA + RT	21	1.90 (0.79)	1.30 (0.37)	-0.60 (0.64)	-1.62	-0.89 - -0.31	<0.001	
Freeway space mean score Recall 1 year	Recall 1 month	no RA + RT	11	3.55 (1.37)	2.18 (0.75)	-1.36 (1.12)	-1.81	-2.12 - -0.61	0.002
	RA + RT	13	3.54 (1.76)	2.31 (1.11)	-1.23 (1.36)	-1.11	-2.06 - -0.41	0.007	
	no RA + RT	19	3.84 (1.46)	2.11 (0.74)	-1.74 (1.33)	-2.35	-2.38 - -1.10	<0.001	
	RA + RT	21	3.81 (1.81)	2.71 (1.01)	-1.10 (1.38)	-1.09	-1.72 - -0.47	0.002	



3

RANDOMIZED CONTROLLED TRIAL ON THE PERFORMANCE OF DIRECT AND INDIRECT COMPOSITE RESTORATIONS IN PATIENTS WITH SEVERE TOOTH WEAR

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ABSTRACT

Objectives: The study aimed to evaluate survival and failure behavior of Direct Composite Restorations (DCR) and Indirect Composite Restorations (ICR) on molars and anterior teeth, in a Randomized Controlled Trial (RCT).

Methods: Patients with generalized severe tooth wear were included, and randomly assigned to one of 2 protocols: (1) DCR: All teeth were restored with directly applied micro-hybrid composite restorations (Clearfil AP-X, Kuraray) for load bearing areas and nano-hybrid composite restorations (IPS Empress Direct, Ivoclar Vivadent) for buccal veneers; (2) ICR: First molars were restored with indirect composite *'tabletop'* restorations and maxillary anterior teeth were restored with indirect palatal veneer restorations (Clearfil Estenia C&B, cemented with Panavia F, Kuraray). Remaining teeth were restored directly. Restorations were evaluated after 3 years, focusing on clinical acceptability. Statistical analysis was performed using Kaplan Meier curves, Annual Failure Rates (AFRs), and univariate Cox regression analyses ($p<0.05$).

Results: 41 patients (age: 36.6 ± 6.6y) were evaluated after 3 years (40.0 ± 2.2m). 408 restorations on first molars and palatal veneers on maxillary anterior teeth were part of this RCT, with 220 DCRs and 188 ICRs. No differences in survival between treatment modality for palatal veneers for any failure criteria were found. Tabletop restorations on first molars showed a considerable higher failure rate for ICR compared to DCR ($p=0.026$, HR: 3.37, 95%CI= 1.16-9.81).

Significance: In this RCT, directly applied composite restorations showed superior behavior compared to the indirect composite restorations, when used in the molar region.

1 INTRODUCTION

Tooth wear is a physiological phenomenon that, when becoming severe or pathological [1], can lead to impaired dental attractiveness, pain, and reduced quality of life [2] or may compromise the prognosis of healthy oral functioning of the dentition. Preferably, the management of tooth wear is focused on prevention, counseling and monitoring [1]. When tooth wear has led to functional or aesthetical problems a restorative treatment plan should be discussed with the patient, which is based on the approach of minimally invasive interventions [1,3,4]. Several techniques have been described to rehabilitate a worn dentition using direct composite restorations [5-11], indirect restorations of composite resin [12], lithium disilicate [13], polymer infiltrated ceramic network (PICN) [14,15], and combined techniques [16-18]. However, the available clinical evidence for any restorative approach of the worn dentition is still limited and a systematic review was not conclusive on which materials and techniques are preferred [19].

In cases of generalized severe tooth wear, minimally invasive rehabilitation of the dentition involves restoring all teeth in an increased vertical dimension of occlusion (VDO), which is a challenging procedure for the dentist. When composites are applied directly, advanced operator skills are required to build up all teeth while for indirect procedures the treatment might be less technically demanding, as restorations are designed and produced extra-orally.

Of the limited number of available clinical studies, most are extended case reports [6,11,17,18], retrospective studies [7], or uncontrolled trials [9]. Recently, a large prospective study was published that included 35 patients with generalized tooth wear. All teeth were treated with direct composite restorations in increased VDO and the reported annual failure rate was around 3% after 3.5 years [8]. According to a systematic review, direct composite has been studied most frequently and modern adhesives and hybrid composites show acceptable results [19]. Another systematic review showed that the total intervention rate of direct composite restorations placed in patients with tooth wear was ranging between 0.8-17.9% [20], showing a large variation between studies, which makes it difficult to make solid conclusions. It underlines the multifactorial factors involved in these high-risk patients.

So far only one randomized controlled trial has been published, comparing microfilled direct and microfilled indirect composite restorations in 16 patients with tooth wear receiving a total of 32 restorations [12]. After up to 3 years, this study showed poor success for both direct (50%) and indirect restorations (50%). Also, in the control group consisting of patients without tooth wear, restorations showed

relatively poor performance at (80% success, which is markedly lower than other studies on large composite restorations, where failure rates of approximately up to 3% were found [21,22]. This indicates that the results of the randomized clinical trial should be interpreted with caution.

Recently, two clinical studies on the success of indirect restorations showed very satisfactory success of 100% for lithium disilicate partial crowns using a moderately invasive concept in 7 patients [13], and 93% for PICN restorations placed in a non-invasive concept in 7 patients [15]. A more invasive treatment with full zirconia crowns in anterior teeth also showed a satisfying performance although no failure rate was reported [23]. Both the technical advantage for the operator and the success of indirect restorations in these studies suggest a place for indirect restorations in the rehabilitation of severe tooth wear.

This study aimed to evaluate in a randomized trial, in patients with moderate to severe tooth wear in need for rehabilitation in increased VDO, the survival and failure behavior of minimally invasive direct and indirect composite resin restorations.

2 MATERIALS AND METHODS

Inclusion and randomization

This randomized controlled trial was designed in accordance with the Declaration of Helsinki (1964). The design and protocol were approved by the local ethics committee (CMO Arnhem-Nijmegen file nr. NL31371.091.10). The study was registered on ClinicalTrials.gov (Identifier: NCT04326816) after completion of the observation time. Patients were referred by their general practitioner to the Radboud Tooth Wear Project at the Department of Dentistry of the Radboud university medical center in Nijmegen (The Netherlands). Inclusion was based on the following criteria: a) Patients age ≥18 years; b) Generalized moderate to severe tooth wear with patient demand for treatment (TWI ≥ 2 [24]); c) Full dental arches, although one missing tooth in the posterior area was allowed d) Estimated need for an increase in VDO ≥3mm in the first molar region. Exclusion criteria: a) Limited mouth opening; b) (History of) Temporomandibular dysfunction; c) Advanced periodontitis, deep caries lesions, or multiple large restorations including teeth with endodontic problems; d) Local or systemic conditions contra-indicating dental treatment. Patients with specific individual risk factors, such as parafunctional

habits of grinding/clenching or patients with GORD (Gastro-Oesophageal Reflux Disease), were not excluded. A sample size calculation based on an assumed 15% difference in survival resulted in a group size of 75.

At first intake, patients were briefly assessed for matching inclusion criteria, and in that case received an information package. After acquiring written informed consent, patients were allocated randomly to either direct (DCR) or indirect composite restorations (ICR) using a sealed envelope. As full indirect composite treatment was not at the time a standard treatment, in the Netherlands, resulting in difficulty in insurance coverage, a hybrid approach was used in which a limited number of occlusion determining teeth were selected for indirect restorations, with remaining teeth restored directly. This resulted in experimental restorations only on first molars and upper anterior teeth (palatal surface). All remaining teeth were restored with direct composite restorations according to the same protocol as DCR, but these restorations were not part of this randomized controlled trial. The treatment protocols are described in detail below. The trial design had an intended allocation ratio of 1:1. Block randomization was used with a block size of eight.

Patients were assigned to one of 7 operators with the intention to evenly divide the number of patients on operators. All operators were dentists experienced in adhesive dentistry from the Department of Dentistry of the Radboud university medical center and participated in multiple calibration sessions for the clinical procedures of both protocols. At baseline, intra-oral examination, photographs, full-arch stone cast models, bitewings, and, when indicated, a panoramic radiograph were used to document patient data. Using this information, matching inclusion and exclusion criteria could be definitively determined, and some previously included patients had to be excluded.

Establishing the new VDO

The increased Vertical Dimension of Occlusion (VDO) needed to obtain sufficient interdental space for the restorations was estimated by two operators (NO and CK) on a consensus basis. To determine the increase, the height loss of those teeth with the largest amount of wear (commonly the first molar) was estimated from the models that were mounted in an articulator. The possibility to lengthen upper and lower anterior teeth was also established. It was assessed clinically by an intra-oral mock-up on the maxilla from canine to canine, in order to obtain consent from the patient for the expected aesthetic appearance. Deficient existing composite restorations and all amalgam restorations were replaced by composite restorations.

Restorative procedures

Direct composite restorations (DCR)

Restorations were placed without preparation of teeth, when possible. In cases of sharp occlusal edges, a minimally invasive preparation was performed. Rubberdam or cotton rolls and suction devices were used for moisture control. Appropriate matrix systems and wedges were used to build up the teeth, at the discretion of the operator. For bonding, a 3-step etch-and-rinse adhesive was applied according to the manufacturer's instructions, using 37% phosphoric acid (DMG, Hamburg, Germany), Clearfil SA Primer, and Clearfil Photobond (Kuraray Noritake Dental, Tokyo, Japan). A micro-hybrid composite (Clearfil AP-X, Kuraray) was used for posterior restorations and palatal/lingual veneer restorations on anterior teeth. Restorations were placed according to the DSO-technique (Direct Shaping by Occlusion, including biting in occlusion on soft composite before polymerization) [25]. In maxillary and mandibular anterior teeth, buccal direct veneer restorations were placed using IPS Empress Direct nano-hybrid composite (Ivoclar Vivadent, Schaan, Liechtenstein) with the same bonding system as described above.

Indirect composite restorations (ICR)

First molars and maxillary anterior teeth in the ICR group were restored with indirectly fabricated tabletop restorations (molars) and palatal veneers (maxillary anterior teeth). In the absence of a first molar, the second molar and its antagonist were used. Preparation of the teeth for indirect restorations was limited to small resistance grooves or pits when necessary for proper seating of indirect restorations and removal of sharp edges to avoid concentration of stresses. All indirect restorations were manufactured using Clearfil Estenia C&B, a micro-hybrid indirect composite (Kuraray). Die stone models made from silicone impressions (Virtual 380, heavy and light body, Ivoclar Vivadent) were used for laboratory manufacturing of the indirect composite restorations in the previously assessed increased VDO. In the dental lab, these indirect restorations were built up in increments. Each increment was light-cured for 30 sec. Final restorations were further light-cured for 9 minutes. Then all indirect restorations were heated in an oven for 15-20 min at a temperature of 110-120 °C to promote further polymerization, according to the manufacturer's instructions.

Adhesive surfaces of the restorations were air-abraded with aluminum-oxide powder (50 µm) for 10 sec by the dental technician (Goedegebuure tandtechniek, Ede, NL). Rubberdam or cotton rolls were used for moisture control during cementation. Seating of indirect restorations was checked intraorally, followed by cleaning of its adhesive surface with phosphoric acid 37% and application of silane

(Clearfil Ceramic Primer, Kuraray). The adhesive surface of the abutment tooth was air-abraded using CoJet sand (30 µm, 3M, Seefeld, Germany) in case of an existing composite restoration. Later, the adhesive surface of the abutment tooth was etched with phosphoric acid (37%) and then ED-primer II (Kuraray) was applied and gently air-dried. Finally, restorations were cemented, according to the manufacturer's instructions, using Panavia F (Kuraray) and finished using discs and finishing burs. In anterior teeth, a buccal direct veneer restoration was placed in a subsequent session using IPS Empress Direct nano-hybrid composite (Ivoclar Vivadent). For optimal bonding to the indirect Estenia palatal veneers, the surface was air-abraded (CoJet, 3M) and a silane coupling agent (Clearfil Porcelain Activator, Kuraray) was used, additional to the bonding procedure with Clearfil SA Primer, and Clearfil Photobond (Kuraray).

No acrylic night guards were advised immediately after treatment. Patients revisited our clinic 1 month after restorative treatment for final adjustments (polishing of restorations and occlusal adjustments for a balanced occlusal relationship).

Follow-up

Recall appointments were scheduled at 1 and 3 years after treatment. Follow-up of up to 3.5 years was considered acceptable. Follow-up after 3.5 years was censored to 3.5 years. The dentition was documented using intra-oral examination and intra-oral photographs. Restorations were checked on clinical acceptability, focusing on functional (debond, fracture, adaptation, anatomy), biological (caries, endodontic treatment), and aesthetic conditions. Restorations needing minor refurbishments by polishing due to discoloration or roughness were not considered as failures. The reason for intervention was recorded, as was its date and category. Failures were divided into three categories: F1) Restorations with severe deficiencies, *e.g.*, extensive or multiple fractures, that were replaced or in case of loss of the tooth; F2) Restorations with localized deficiencies, *e.g.*, adhesive fractures, that were repaired; F3) Restorations with small material chippings that needed refurbishment by polishing. Moreover, as all patients visited their General Dental Practitioner (GDP) for regular check-ups, the GDP's were contacted to share information about any intervention related to the restorations in the period of follow up.

Statistical analyses

The longevity of restorations was explored with survival tables and Kaplan Meier graphs. Out of the survival tables, mean Annual Failure Rates (AFR) over 3 years were calculated according to the formula: $AFR = 1 - \sqrt[3]{S}$ in which 'S' is the level of restorations not meeting the failure criteria. AFRs were separately calculated for the different failure levels (replacement/tooth loss, repair, and refurbishment).

For analysis of restoration survival, a univariate Cox model using a shared frailty term was used to adjust for the dependency of data, as multiple restorations were clustered within one patient. These analyses were done using the library survival within the R software (v 3.6.3). Differences between direct (DCR) and indirect restorations (ICR) were analyzed in accordance with the Intention-To-Treat principle. Survival analyses were performed for comparing the experimental direct restorations (on first molars and palatal veneers on maxillary anterior teeth) with the indirect composite restorations, for the 3 levels of failure. Later, a subgroup analysis was conducted to evaluate the effect of treatment modality on maxillary anterior teeth and first molars, separately. Furthermore, descriptive analyses were completed to report about failures of restorations not involved in the randomized controlled trial. The alpha was set at $p = 0.05$.

3 RESULTS

Inclusion took place between February 2011 and October 2014 and was performed by a researcher not involved in the treatment (BL). Treatment was conducted between October 2011 and July 2015. As an interim analysis by the statistician (EB) showed that the failure rate of indirect restorations was considerable and already reached statistical significance, it was decided to stop inclusion. At that moment, randomization had led to an allocation of 25 patients to the DCR-procedure and 24 patients to the ICR-procedure. 3 participants from the DCR-procedure had to be excluded before restoration because inclusion criteria were not met (1x multiple missing teeth, 2x VDO<3mm). Also, 4 patients allocated to the ICR-procedure were excluded before restoration, as inclusion criteria were not met (1x deep caries lesions, 1x multiple missing teeth, 2x VDO<3mm). Blinding could not be implemented, neither for patients nor for operators, for the used treatment techniques have obvious differences. In total, 42 patients were restoratively treated (36 males, 6 females). 1 (female) patient, allocated to the ICR-procedure, was regarded as lost to follow-up as no follow-up data were available. The flow chart of the clinical study is shown in Figure 1. All other patients were recalled after 1-year, but 4 patients could not be recalled after 3-years. Their data of the GDP (after more than 5 years) could be retrieved. Therefore, these patients were included in the analyses, and their observation time was censored to 3.5 years. 2 GDP-files could not be retrieved, see supplementary data.

Statistical analysis was conducted for 41 patients; 22 patients (3 female) allocated to the DCR-procedure (mean age: 36.6 ± 8.0) years), and 19 (2 female) patients allocated to the ICR-procedure (mean age: 36.7 ± 4.7 years). The mean observation

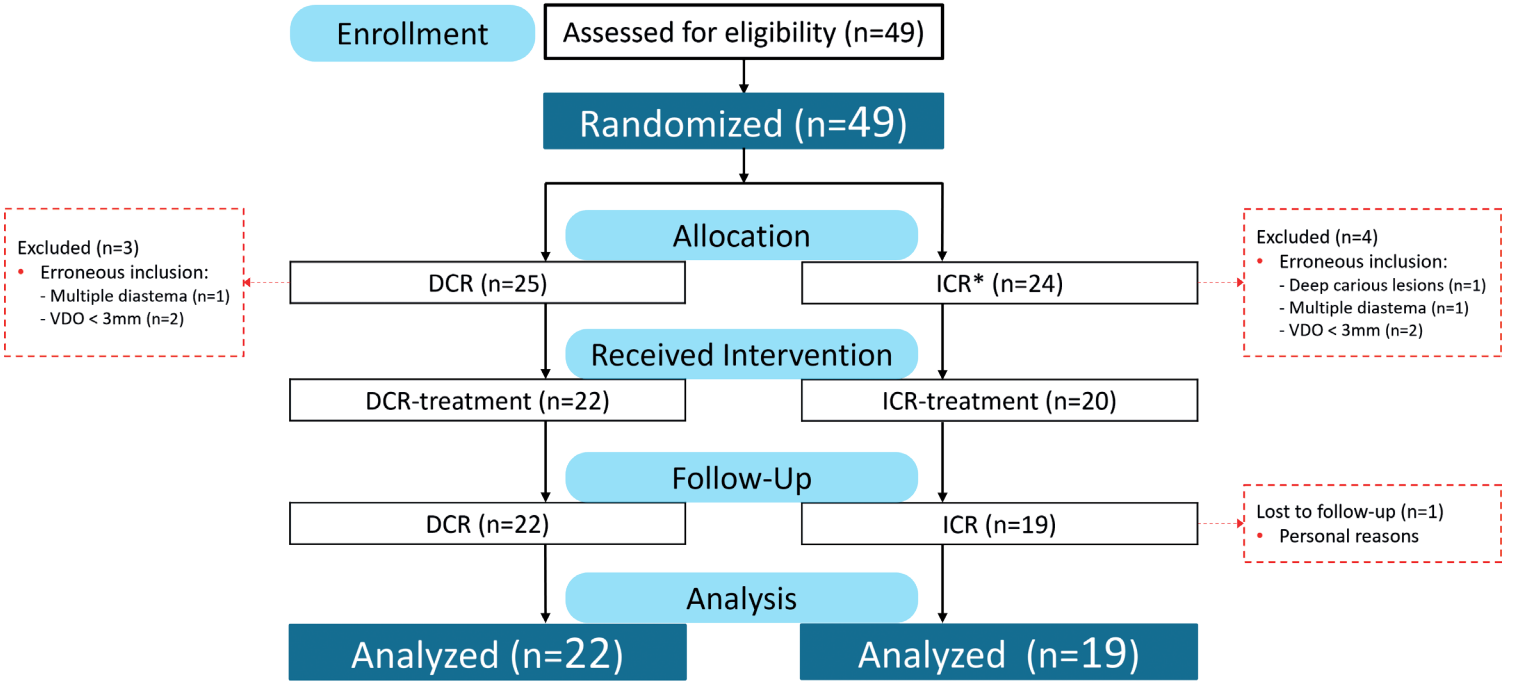

Figure 1: Flowchart of the handling of patients regarding allotted treatment, treatment, follow-up, and analysis. Two patients allocated to the ICR treatment actually received the DCR treatment for financial reasons. Analyses were performed conform the intention-to-treat principle.

time, including censoring, was 39.5 ± 2.5 months (range: 34.8 to 42.0) and 40.5 ± 1.7 (range: 36.4 to 42.0) months for the DCR-group and ICR-group, respectively. Due to financial reasons, 2 patients allocated to the ICR-procedure, actually received the DCR-procedure (Fig 1). Statistical analysis was performed according to the Intention-To-Treat principle. No adverse events occurred in both treatment groups. The average number of restorations per patient was 41 (± 5). Nightguards were made for 3 patients after the 1-year recall, as multiple fractures were seen and patients expressed their wish for additional protection of a nightguard (see supplementary data).

Overall, 1,660 restorations were placed, of which 408 restorations were evaluated as part of this randomized controlled trial. In the DCR-group, 220 directly applied restorations were placed, of which 88 restorations were direct 'tabletops' and 132 were direct palatal veneers. The ICR-group consisted of 188 indirect restorations, of which 76 restorations were 'tabletops' placed on first molars (incidentally second molars) and 112 indirect palatal veneers on maxillary anterior teeth. 62 interventions occurred within the observation time. As only 1 restoration was completely lost through tooth extraction, Cox regression to compare treatment modalities for this failure criteria (F1) was not sensible. 34 restorations were repaired (F2) and 27 restorations were refurbished (F3). 52 (out of 62) interventions were related to fracture. Significant differences between the treatment techniques for the second and third failure criteria were found. The hazard ratio of ICR for the second failure criteria, including failures on level F1 and F2, was 3.33 ($p=0.011$, 95%CI= 1.32-8.36). The hazard ratio of ICR for the third failure criteria, including failures on all levels, was 2.85 ($p<0.001$, 95%CI= 1.50-5.44). Cox regression analyses and Annual Failure Rates (AFR) are described in Table 2.

Table 1 - Overview of all failures and their specifics after 3 years for the subset of palatal veneers on maxillary anterior teeth and tabletop restorations on first molars

			Functional		Biological			Unknown	Total
			Fracture	Anatomy	Caries	Endodontic treatment	Extraction		
Maxillary anterior teeth (n=262)	Direct (n=132)	F1							0
		F2	2						2
		F3	1						1
	Indirect (n=112)	F1							0
		F2	5	1					6
		F3							0
First molars (n=152)	Direct (n=88)	F1					1		1
		F2	1			1		4	6
		F3	7						7
	Indirect (n=76)	F1							0
		F2	17		1			2	20
		F3	19						19
Overall			50	1	1	1	1	6	62

Subgroup analyses were conducted to evaluate the effect of the treatment technique for palatal veneers and tabletops, separately. 132 directly applied palatal veneers were compared with 112 indirect palatal veneers and 88 directly applied tabletops were compared with 76 indirect tabletops. The palatal veneers were evaluated for the second and third failure criteria. 9 palatal veneer restorations received an intervention, with 6 repairs (F2) on indirect palatal veneers and 2 repairs (F2) and 1 refurbishment (F3) on the directly applied palatal veneers. No differences in survival between treatment modality for palatal veneers for any failure criteria were found. Tabletop restorations on first molars (incidentally second molars) showed a considerable higher failure rate for ICR compared to DCR for both the second (F2 and F1) (p=0.026, HR: 3.37, 95%CI= 1.16-9.81) and third failure criteria (F3, F2, and F1)(p=0.002, HR=3.21, 95%CI= 1.55-6.61). Kaplan-Meier curves are shown in Figure 2 and Figure 3.

Furthermore, 1,252 restorations were placed on remaining teeth. 77 interventions were registered. 6 restorations were lost/replaced (F1), 42 restorations were repaired (F2), and 29 restorations were refurbished (F3). 48 interventions were related to fracture, see table 3

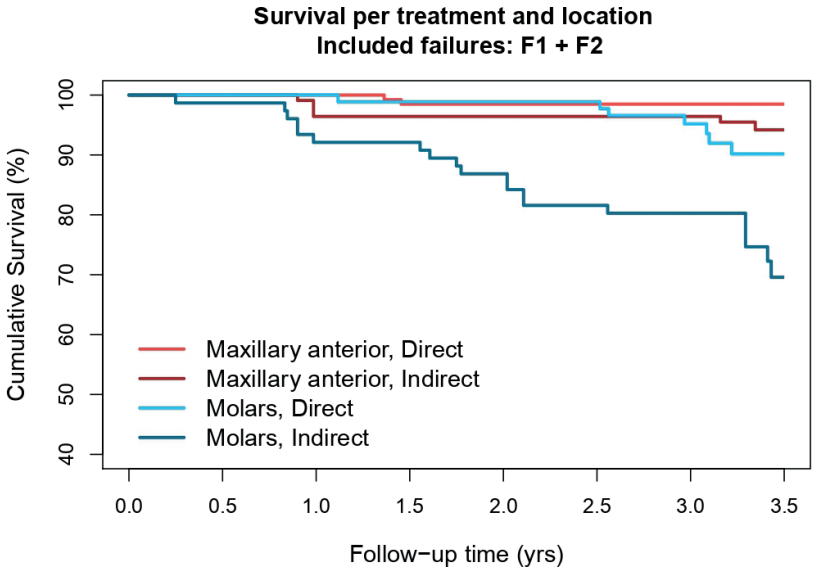

Figure 2: KM curves of all subgroups based on the second failure criteria (F2 + F1)

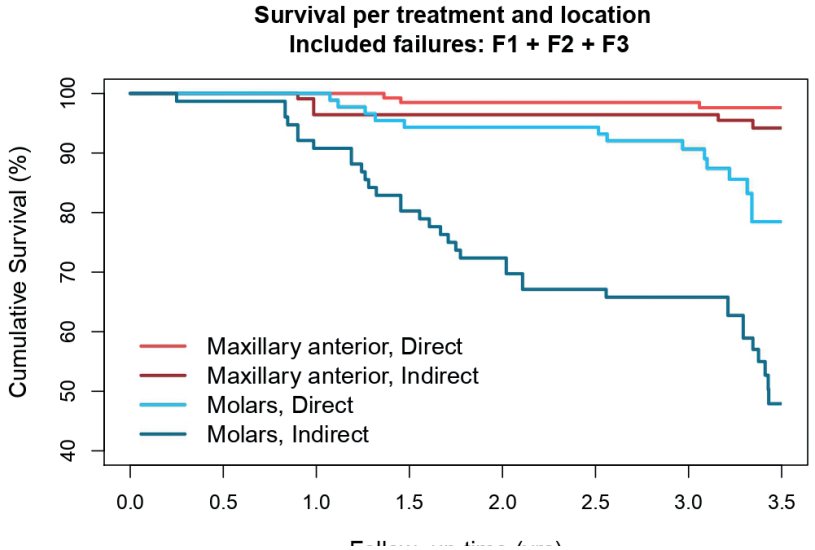

Figure 3: KM curves of all subgroups based on the third failure criteria (F3 + F2 + F1)

Table 2 – Univariate Cox Regression analyses and Annual Failure Rates

MAIN ANALYSES - all restorations part of the RCT					Univariate Cox Regression		
		Restorations (n)	Events (n)	AFR (%)	P value	HR	95% CI
F1	All restorations in DCR-group	220	1	0.2	n.a.	n.a.	n.a.
	All restorations in ICR-group	180	0	0	n.a.	n.a.	n.a.
F1 + F2	All restorations in DCR-group	220	9	1.3	-	1.00	-
	All restorations in ICR-group	180	26	4.0	0.011	3.33	1.32 - 8.36
F1 + F2 + F3	All restorations in DCR-group	220	17	2.2	-	1.00	-
	All restorations in ICR-group	180	41	7.0	0.001	2.85	1.50 - 5.44
SUBGROUP ANALYSES – all restorations part of the RCT split analyses for location							
		Restorations (n)	Events (n)	AFR (%)	P value	HR	95% CI
F1	All palatal veneers in the DCR-group	132	0	0	n.a.	n.a.	n.a.
	All palatal veneers in the ICR-group	112	0	0	n.a.	n.a.	n.a.
	All tabletops in the DCR-group	88	1	0.5	n.a.	n.a.	n.a.
	All tabletops in the ICR-group	76	0	0	n.a.	n.a.	n.a.
F1 + F2	All palatal veneers in the DCR-group	132	2	0.5	-	1.00	-
	All palatal veneers in the ICR-group	112	6	1.8	0.153	3.43	0.63 - 18.58
	All tabletops in the DCR-group	88	7	3.2	-	1.00	1
	All tabletops in the ICR-group	76	20	8.5	0.026	3.37	1.16 - 9.81
F1 + F2 + F3	All palatal veneers in the DCR-group	132	3	0.7	-	1.00	-
	All palatal veneers in the ICR-group	112	6	1.8	0.289	2.27	0.50 – 10.31
	All tabletops in the DCR-group	88	14	5.4	-	1.00	1
	All tabletops in the ICR-group	76	35	15.5	0.002	3.20	1.55 – 6.61
OBSERVATIONAL DATA - All restorations not part of the RCT							
		Restorations (n)	Events (n)	AFR (%)			
F1	Directly applied restorations on teeth not part of RCT	1252	6	0.2			
F1 + F2	Directly applied restorations on teeth not part of RCT	1252	48	1.3			
F1 + F2 + F3	Directly applied restorations on teeth not part of RCT	1252	71	1.8			

Table 3 – Overview of all interventions on restorations not part of the RCT

		Functional			Biological			Unknown	Total
		Fracture	Anatomy	Debond	Caries	Endodontic treatment	Extraction		
Directly applied restorations (n=1252)	F1			5	1				6
	F2	22	10		6	1		3	42
	F3	26						3	29
Total		48	10	5	7	1	0	6	77

4 DISCUSSION

In this study, we analyzed the clinical performance of restorative rehabilitations for patients with generalized moderate and severe tooth wear in increased VDO using minimally invasive direct and indirect composite resin restorations. Indirect composite restorations showed an inferior survival compared to direct composite restorations. This effect was mainly found in the molar region.

In the Netherlands, many severe tooth wear patients are treated with direct composites as these treatments will usually be (partially) reimbursed by public health insurance. As dentists may prefer to use indirect composite restorations on (some) teeth to facilitate establishing the increased VDO, the protocols that we used in this study reflect the standard of care for severe tooth wear patients in the Netherlands with full rehabilitation in increased VDO. The protocols comprise restoration of all teeth either with only DCR, using the DSO technique [25], or with a protocol combining both ICR on anterior teeth and on molars, to establish the occlusal relationship in increased VDO, and restoration of remaining teeth with DCR. For the RCT, only the teeth receiving different treatment in DCR- and ICR-patients were analyzed.

For the outcome, we have distinguished between three levels of failure (F1, F2 and F3), see Figs. 4 and 5. From the perspective of care, differences between repair and replacement are important outcomes as repair can be considered as a survival of the restoration [26]. Chippings were also reported as they may be important for reporting on differences between materials or techniques, without having an impact on the delivered care. The main outcome from the analysis is that for molars, the performance of the indirect composite restorations was significantly worse compared to the direct restorations. The high annual failure rate of $8.5_{(F2)}$-$15.5_{(F3)}$% for indirect molar restorations and $3.2_{(F2)}$-$5.4_{(F3)}$% for direct restorations) led to an earlier end of the inclusion process than anticipated.

Cox regression analysis showed a significantly higher risk for failure (HR 3.2-3.4) of indirect restorations in the molar teeth. Another RCT in regular (non-tooth

wear) patients comparing the performance of large Clearfil Estenia C&B indirect composite restorations and large APX direct composite restorations on premolars with cusp fractures, showed a similar (although non-significant) trend as found in the present study [27]. In that same study, AFRs were lower, illustrating the high-risk profile of the present patient population. Direct and indirect restorations showed comparable performance in palatal restorations on anterior teeth. Although the same trend is shown as for molar restorations, the difference is marginal. Another protocol that was evaluated in a case series on tooth wear patients using palatal composite veneers also showed good performance [18].

The explanation for the differences in performance in the molar restorations could be material-specific. The applied composites are both heavily filled hybrid composites with relatively high E-moduli. 15.3 GPa is reported for Clearfil AP-X while for Clearfil Estenia C&B 28.6 GPa is reported by the manufacturer although 14.0 GPa is reported by De Kok et al., [28]. Therefore, it is doubtful whether these material properties have played a major role in the failure behavior. Another reason for the higher failure rate of indirect restorations in the molar region might be the manufacturing process and related differences in layer thickness. For most materials, a thicker layer offers more strength, although this property can be material-specific [29]. As stated by the manufacturer of Clearfil Estenia C&B, tabletop restorations should be ≥1.5 mm in thickness, which was also the guideline for the dental technician and in accordance with patient exclusion rules for patients. Still, we did not check all indirect restorations for thickness before placement, other than the clinical judgment of the operator. It may be that some restorations had incipient weak spots due to insufficient thickness. For direct composites, minimal thickness seems less important than indirectly placed restorations [30].

A third possible explanation could be the different, more complex, and thicker adhesive layer for the indirect restorations, including adhesives and adhesive cement resulting in multiple interfaces, while for direct composites, only one thin interface of a 3-step etch-and-rinse adhesive is applied. Possibly, all three factors contributed to the present findings.

Overall, the present study shows a satisfactory survival of restorative work that is placed in severe tooth wear patients for direct composite restorations (AFR $_{(F2\text{-}F3)}$= 0.5–0.7% for anterior direct restorations and 3.2–5.4% for posterior direct restorations) and indirect anterior composite restorations (AFR = 1.8%), but not for indirect composite restorations in molars (AFR $_{(F2\text{-}F3)}$ = 8.5–15.5%). Our results confirm previous studies indicating that direct composites are suitable for restoring tooth wear cases in increased VDO [6-11,17,19,20], with the exception of one RCT [12]. The

outcome of that RCT may be related to the choice of material (microfilled direct and indirect composites) or unknown operator related factors. The present study shows, again in accordance with the outcomes of these other studies, that fracture and chipping, are the main reasons for failure, resulting in a need for maintenance work [31]. However, in these high-risk patients, chipping and fractures also may occur for indirect materials [23]. Therefore, in the future, direct restorations should be compared to other materials/techniques like CAD/CAM composite, polymer infiltrated ceramic network, and lithium disilicate as well as full zirconia restorations in this specific group of patients. Overall, as it can be assumed that for these high-risk patients with severe tooth wear, any restorative treatment is at best temporary, a minimally invasive technique also for indirect restorations should be applied.

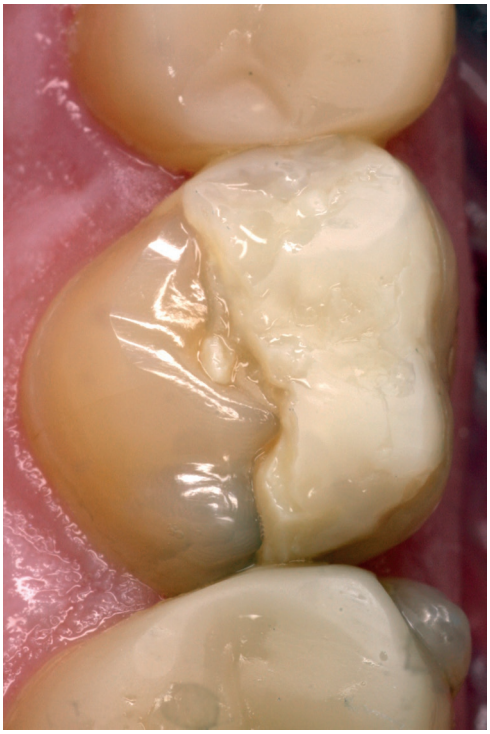

Figure 4: Example of restoration failure conform the second failure criteria (F2)

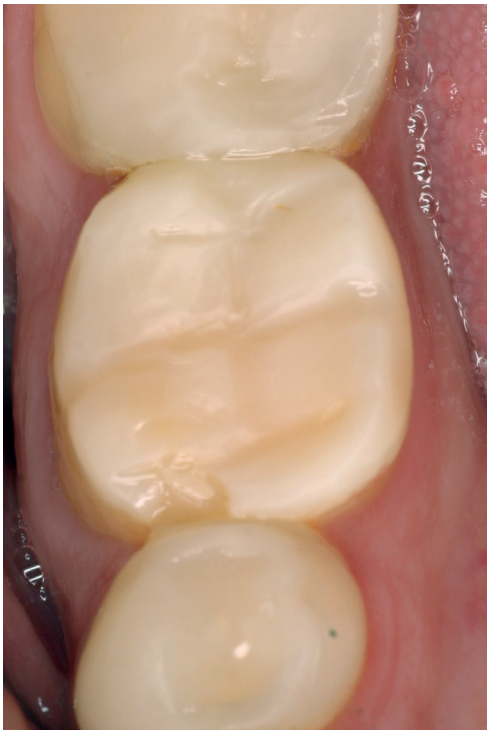

Figure 5: Example of restoration failure conform third failure criteria (F3)

5 CONCLUSION

This randomized controlled trial showed that for molar restorations, the applied indirect composite is not suitable for use in severe tooth wear patients. Indirect composite restorations in anterior teeth and direct composite restorations for anterior and posterior teeth showed a satisfying performance after a 3-year observation period.

6 ACKNOWLEDGEMENTS

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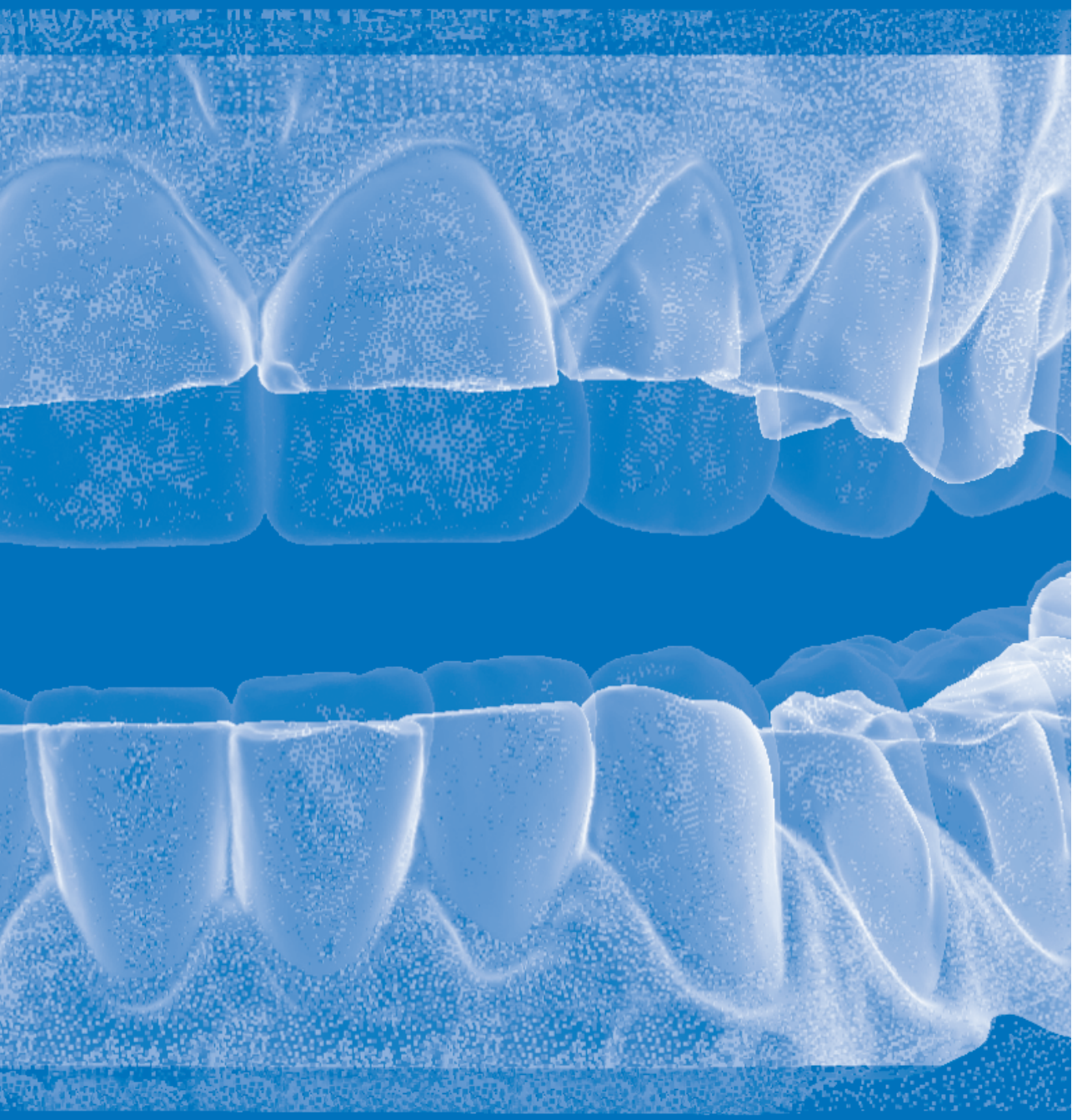

4

REHABILITATION OF THE WORN DENTITION WITH CAD/CAM RESTORATIONS: A CASE REPORT

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ABSTRACT

Purpose: The aim of this case report is to describe the digital workflow that was applied for restoring a severely worn dentition with minimally invasive CAD/CAM resin nano ceramic restorations.

Materials and Methods: A 40-year-old male with good general health and full arch dentition suffered from dentine hypersensitivity and had a demand to improve the aesthetics of his worn anterior teeth. The tooth wear can be described as general, grade 3 according to the Tooth Wear Index [1] with more wear in upper than in lower teeth. Signs and symptoms were typical for a chemical type of wear, with some mechanical wear also apparent. No functional problems, like impaired chewing, were present. On the OHIP-49 questionnaire the patient expressed a reduced quality of life. The goal of the treatment was to reconstruct, as much as possible, anatomical form of the teeth, thereby also improving quality of life.

Results: Due to the considerable volume of lost tooth tissue per tooth the indirect treatment technique using CAD/CAM resin nano ceramic restorations (LAVA Ultimate, 3M) was applied. The seating of the restorations was considered precise.

Conclusion: In the treatment of severe tooth wear, the described digital workflow using CAD/CAM restorations for occluding restorations and direct composite materials in the aesthetic zone is a potential treatment modality that is workable and minimally invasive.

1 INTRODUCTION

Significant clinical symptoms of patients with severe generalized tooth wear include tooth sensitivity, chewing difficulties, impaired aesthetics, and fracture of tooth tissue and dental restorations [2,3]. Given these problems, the outcome of tooth wear management including shared decision making with the patient, can lead to a restorative intervention to rebuild the worn dentition into its original anatomy [2]. Full crowns may be restorations of choice in such rehabilitation [4-6], due to the possibility to design all restorations coherently in one technical procedure and the long years of experiences with indirect restoration techniques in dentistry. However, full-mouth clinical preparation procedures are strenuous and full-coverage crowns go along with high biological and economical investments and are therefore considered as invasive treatments [7]. Moreover, as severe tooth wear patients can be considered as 'high risk' to restoration failure, it can be expected that any restorative treatment is likely to have a limited longevity. While candidates for those full rehabilitations are often relatively young of age, this results in retreatments of increasing complexity.

To minimize the biological price, tapered tooth preparations should be avoided and, as the tooth has already been worn away, one should preserve tooth tissue in order to enable future retreatments with minimal complication risk. Minimal intervention rehabilitations include restorations with direct composites [8-13]. These treatments show satisfying midterm results, although repairs may be necessary in the follow-up according to a recent systematic review [14,15]. Moreover, rehabilitations with direct composite require technical skills of the operator and a considerable clinical working time is needed.

To reduce the demand on the operator's skills, indirect adhesive restorations may offer another treatment modality to restore worn dentitions with minimally invasive techniques. Another advantage compared to the direct techniques may be the more predictable application of the Vertical Dimension of Occlusion (VDO) in the treatment procedure. Recently, encouraging results have been reported using Polymer Infiltrated Ceramic Networks (PICN) manufactured by CAD/CAM techniques for rehabilitation of tooth wear patients, including bruxists, following a minimal invasive protocol [16]. Another recent report showed excellent results with lithiumdisilicate restorations although in that study still a moderately invasive technique was applied including occlusal and proximal reduction of teeth [17].

Hybrid ceramics like resin nano ceramics and PICNs have been developed to combine the advantageous material properties of ceramics, such as wear resistance, and those of composites, such as the dentin-like elastic modulus [18]. These materials

are processed in the milling machine in the maximum polymerized condition, which promotes optimal fit of the restoration since no postprocessing compensation is required. Additionally, the ease of handling of the modestly brittle materials results in a practical milling time per restoration reducing costs. If combined with a 3D-impression made with the intra-oral scanner, a nearly complete digital workflow can be created, which might be beneficial if multiple build-up restorations (e.g. uplays and backings) in one patient have to be produced [16,19].

Today, minimal invasive techniques for the treatment of severe tooth wear may not exclusively be restricted to direct restorations since CAD/CAM processing of combined resin and ceramic materials seem to offer clinical functional materials as well as unsophisticated technical procedures. The aim of this case report is to describe the digital workflow that was applied for restoring a severely worn dentition with minimally invasive CAD/CAM resin nano ceramic restorations.

2 CASE REPORT

The patient is a 40-year-old male with good general health and full arch dentition who worked as a chef in a local restaurant. He was pointed out to the tooth wear by his dentist and was concerned about its progression. At the first appointment, anamnestic information was acquired and the level of tooth wear was documented using intra-oral photographs (Fig. 1). The patient was informed about the multifactorial etiology of tooth wear in general. Parafunctional habits (grinding) and frequent acidic intake, related to his profession, were identified. The patient was not aware of signs of gastroesophageal reflux disease (GERD) at first but acknowledged the presence of mild symptoms later. It was decided to start restorative treatment as the patient had a clear demand for treatment as he suffered from dentine hypersensitivity and wanted to improve the aesthetics of the worn anterior teeth. To reduce progress of clinical symptoms and to optimize long term behavior of restorations, he was advised to limit acidic intake and to use fluoride-rich mouth rinse daily. The patient was also referred to his general practitioner to limit reflux of gastric acid.

No functional problems, like impaired chewing, were present. There were no observable periodontal pockets. Oral hygiene was adequate as there was hardly any visible plaque and no bleeding on probing. Risk assessment for caries was performed and was esteemed low as only a few occlusal composite restorations were present and no carious lesions were detected. He had an Angle Class I molar relation with an active occlusion that could be characterized as group function to both the left and the right side (Fig. 1).

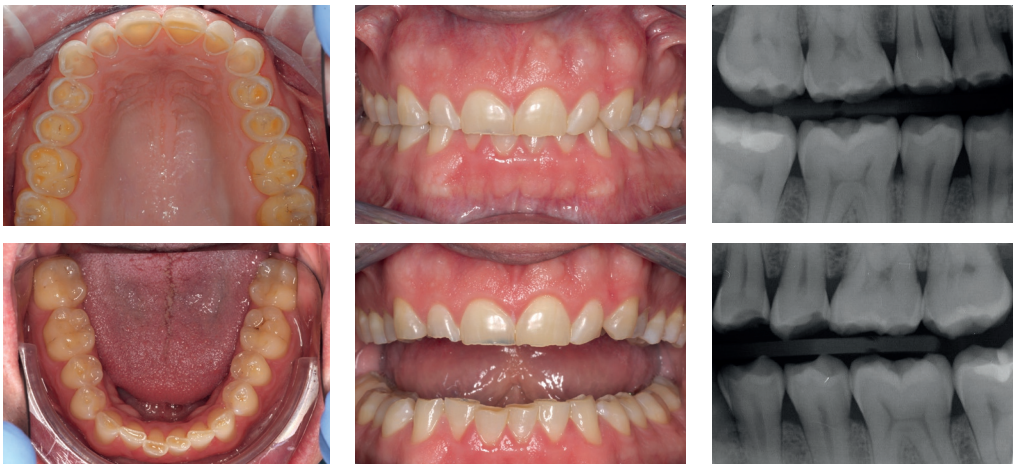

Figure 1: Intraoral photographs and bitewing radiographs at baseline.

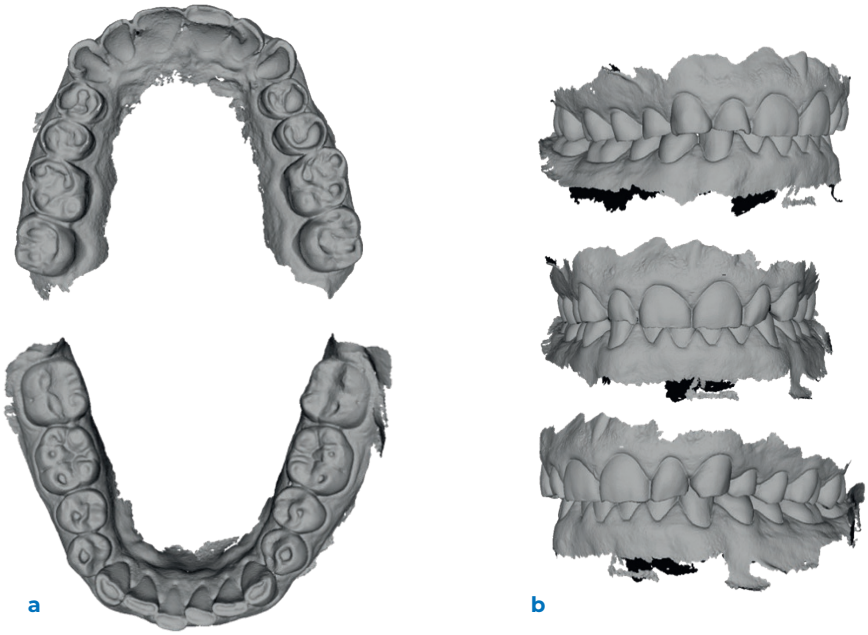

Figure 2: Intraoral 3D scans, occlusal surfaces (a) and maximal occlusion (b)

The tooth wear can be described as general, grade 3 according to the Tooth Wear Index [1] with more wear in the upper than in the lower teeth. Central incisors were worn away for about 2 mm in length. Based on the gingival line of lower front teeth, dentoalveolar compensation was not apparent. Although mechanical wear as etiological factor could not be ruled out, signs and symptoms were typical for a chemical type of wear (eroded palatal surfaces, deep cupping, no wear facets on

occluding surfaces, sensitivity). This is also shown on the intra oral scans (Fig. 2). On the OHIP-49 questionnaire the patient expressed a reduced quality of life.

In this case severe and generalized occlusal wear was present which has resulted in shortening of the teeth. An increase of VDO by restorative rehabilitation was required. The goal of the treatment was to reconstruct, as much as possible, anatomical form of the teeth, thereby also improving quality of life. Due to the considerable volume of lost tooth tissue per tooth it was decided to use the indirect treatment technique using CAD/CAM restorations.

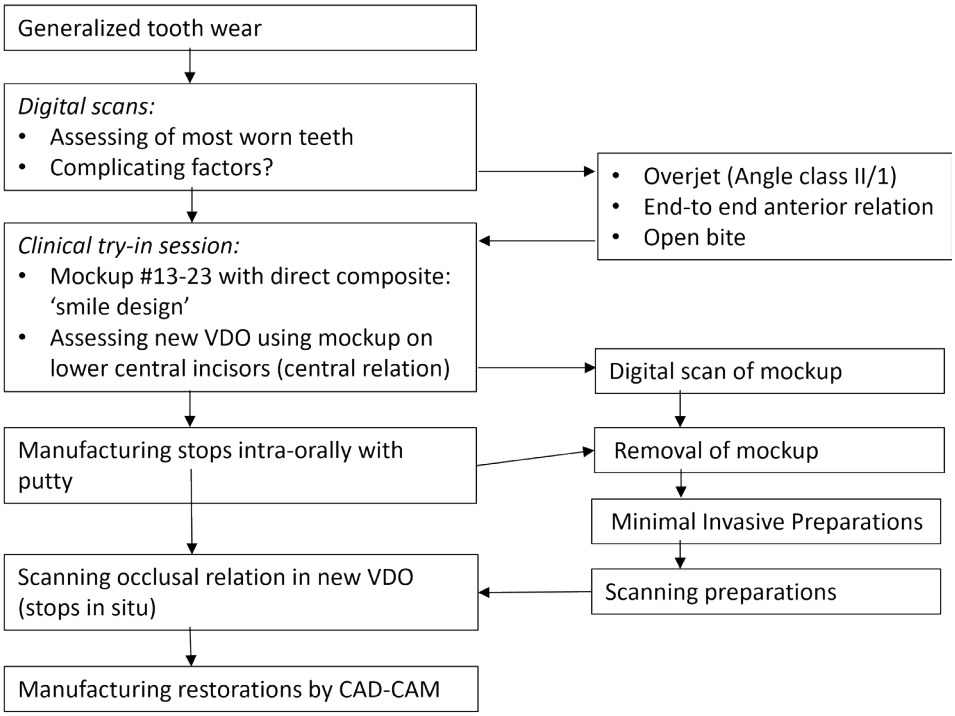

Figure 3: Workflow to determine the new VDO in relation to the clinical procedures.

Clinical tryout session to determine the new VDO

The workflow to determine the VDO that we have used is presented in Fig. 3. The new VDO was estimated based on the lost anatomical shape of the teeth and the necessity to lengthen the upper and lower anterior teeth. Starting point of the rehabilitation was an *in situ* free-hand mockup using direct, unbonded composite anterior veneer restorations according to the lip-generated smile design [20]. We used the mockup to determine whether the lengthening of anterior teeth was clinically applicable and aesthetically satisfactory. To provide the patient a realistic impression

of the expected aesthetic appearance, the mockup included all 6 upper anterior teeth. In this way the location of incisal edges relative to the lip, the smile, and the color of the potential restorations could directly be checked by both operator and patient (Figs. 4a and 4b). After approval of the aesthetics by the patient, the mockup was recorded using a digital pre-op scan (True Def IOS, 3M), serving as guidance for the digital wax-up in a later stage of the procedure.

Then, the estimated new VDO was determined intra-orally by applying a free-hand composite mockup on the central lower incisors (Fig. 4c). By applying composite to palatal surfaces of the upper central incisors we controlled the interocclusal distance at the location of the first molars when the patient was closing along the retruded path. This led to an increase of about 3.5 mm of the VDO (roughly 1.5 mm space for the required thickness of both the upper and lower restorations). This VDO was preserved by making fast-setting, stiff silicon bite blocks (Star VPS, Danville Materials) at the right and left posterior areas, while the patient was in centric relation closing on the anterior mockups (Fig. 4d). After the mockups were removed, composite restorations on occlusal surfaces of teeth numbers 37 and 47 were replaced with direct composite restorations due to deficient margins.

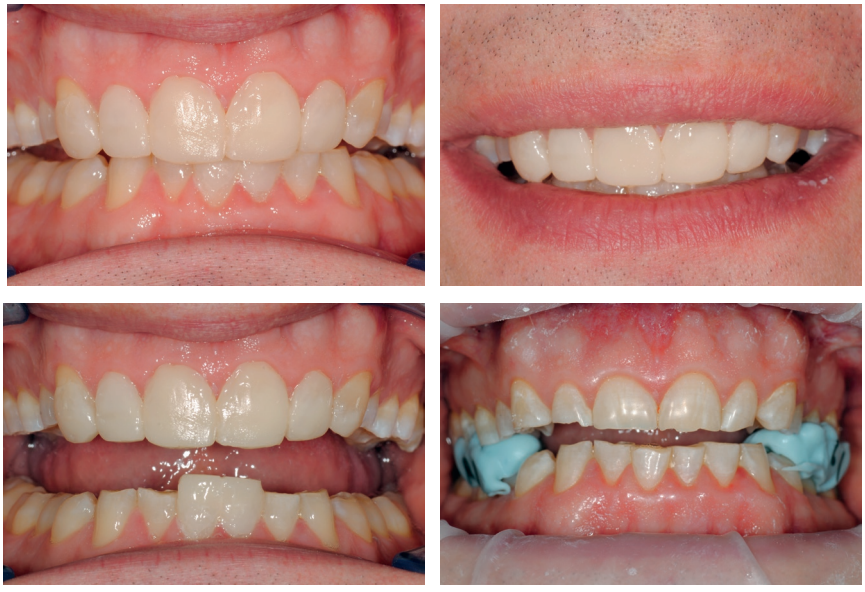

Figure 4: Mockups on the maxillary and mandibular anterior teeth and silicon stops *in situ* to preserve the new VDO.

Preparation and scanning

During the next treatment session all teeth were prepared for indirect restorations: table-tops on posterior teeth, palatal veneers on upper anterior teeth and buccal veneers on lower anterior teeth. Tooth preparation was limited to (1) taking away sharp ridges that could initiate cracks in the covering restoration, and (2) a small chamfer to provide the outline of posterior occlusal surfaces (Fig. 5a).

Digital impressions (True Def IOS, 3M) were made according to the instructions of the manufacturer (Figs 5b and 6a). Restorative surfaces of maxillary anterior teeth were located just supragingivally on the palatal surfaces, so gingival retraction was necessary during scanning for these teeth only. After the upper and lower scans were obtained, the occlusion scans, in increased VDO, were made with the two bite blocks in-situ. In this way, the new VDO was transferred from the clinic to the digital environment. Since hardly any occlusal tooth tissue was removed, temporary restorations were not necessary.

Scans were transferred to the dental laboratory (Elysee Dental, Modern Dental Laboratory, Alphen aan de Rijn, The Netherlands) that designed a fully digital wax-up. The oral and buccal surfaces of the upper anterior teeth were designed according to the scanned mockup (pre-op scan of mockup). At this stage the lower anterior teeth and the second premolars and the second molars, both in the upper and in the lower jaw, were designed (Procedure 1, Fig. 6b). To note, the first premolars and first molars teeth were designed after the placement of the restorations of the second (pre)molars. After approval of the design by the dentist, the veneer restorations including the incisal edges for the anterior teeth and table-top restorations for the posterior teeth were computer aided milled from resin nano ceramic restorative material (LAVA Ultimate®, 3M) in the color A2. restorations).

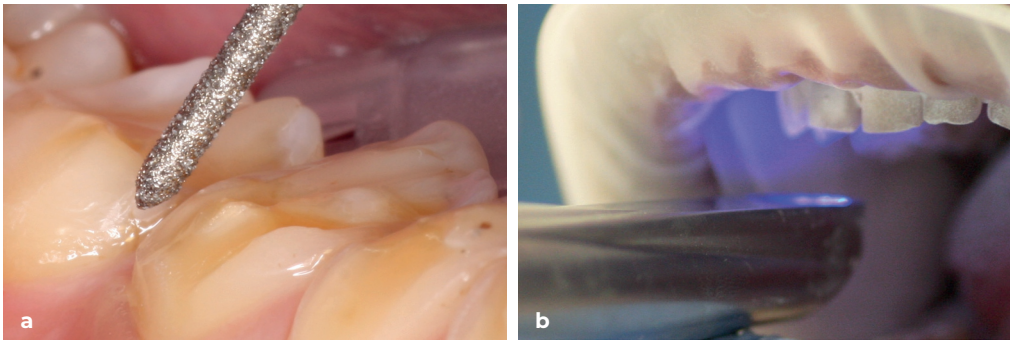

Figure 5 Preparation of teeth (a) and intraoral scanning (b)

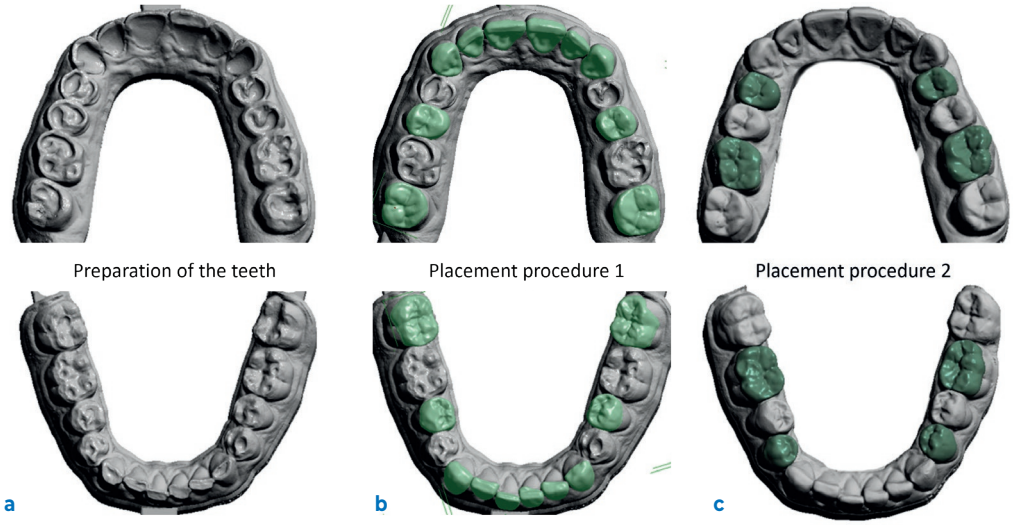

Figure 6: Design of the indirect nanoceramic restorations according to two sequential procedures

Placement procedure 1

For the delivery of the restorations and global check of seating, a printed model was used to fit the milled restorations. The steps before placement included cleaning of the adherent surfaces of the teeth with pumice and rinsing. Restorations were tried-in prior to cementation with the restoration adhered to an adhesive stick (Optra stick, Ivoclar Vivadent, Schaan, Liechtenstein) (Fig. 7). The internal surface of the restorations was sandblasted using SiO_2-coated Al_2O_3 (Cojet, 3M) under 2.5 bar to clean, to roughen and to apply a silicate coating on the surface, followed by a layer of silane (ESPESIL, 3M).

A rubberdam was applied, and a transparent matrix was wrapped around the tooth and fixed with wooden wedges. Total etching was employed to the tooth tissue (Scotchbond Etchant, 3M) for 15 seconds, rinsed and dried by air and bonding agent (Scotchbond Universal, 3M) was applied, gently air-dried and photocured for 10 seconds. The restorations were placed using composite resin cement (RelyX Ultimate, 3M), excess of cement was removed, followed by light-curing for 40 seconds (Bluephase 16i, Ivoclar Vivadent; maximum output 1.600mW/cm^2). Finally, the outline of the restorations was finished using fine diamond burs, finishing disks and points.

In this procedure 1, placement started with the upper central incisors, followed by the lateral incisors, canines, second premolars and second molars. Subsequently,

restorations of the lower anterior teeth were placed in the same sequence. After removing occlusal interferences, the remaining teeth (first premolars and first molars) were cleaned with pumice and preparations adjusted. New fully intra-oral scans including bite registrations were made and sent to the dental laboratory to design and produce the eight remaining indirect restorations for Procedure 2 (Fig 6c).

Placement procedure 2

The patient revisited the clinic about two weeks after placement procedure 1. The procedures to check the seating of the remaining eight restorations and the cementation procedure were identical to Procedure 1. After cementation, all restorations were finished, and occlusion/articulation was checked and corrected when necessary.

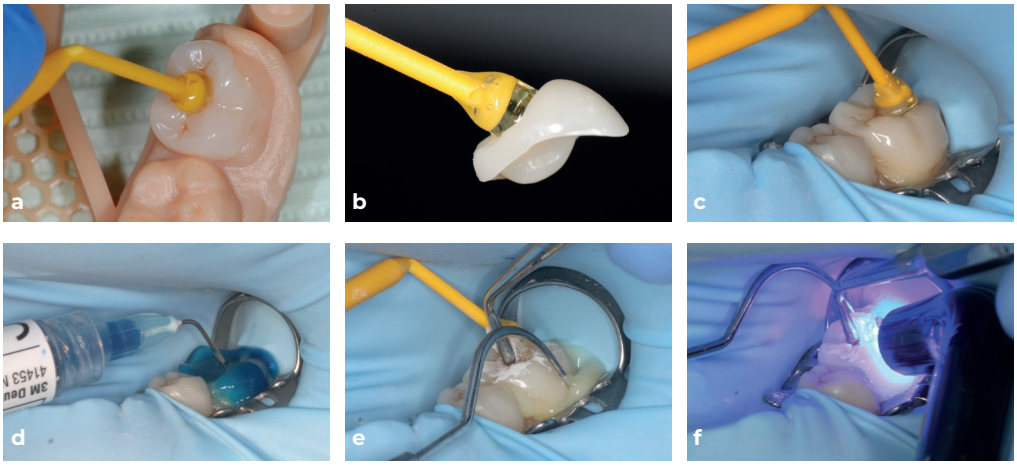

Figure 7: Cementation of the CAD/CAM restorations. a: indirect restoration placed on printed model; b: indirect restoration adhering to adhesive stick; c: try-in of indirect restoration; d: etching of the abutment tooth; e: placement of indirect restoration and removal of excess cement; f: light curing of cement.

Placement procedure 3: direct veneer restorations

The placement of the CAD/CAM indirect restorations was followed by fabrication of direct composite buccal veneer restorations on the upper anterior teeth during placement Procedure 3, one week after Procedure 2. The indirect CAD/CAM palatal veneers were manufactured to their definitive length, which simplified direct veneer placement. After placement of a matrix, the buccal surface of the indirect restorations was roughened with a bur and air-abraded with SiO_2-coated Al_2O_3 (Cojet, 3M). Then the tooth tissue was etched (Scotchbond Etchant, 3M) for 15

seconds, rinsed and dried. A silane was applied (ESPESIL, 3M) and gently air-dried followed by the bonding agent (Scotchbond Universal, 3M) that was applied, gently air-dried and photocured for 10 seconds. The composite resin (Filtek Supreme XTE, 3M) was placed with a multi-layering technique in this case color A2B and A1E. After light-curing the veneers were polished using fine diamond burs, Soflex discs (3M) and rubber polishing disks (Twist DIA, Kuraray Noritake, Japan). Fig. 8 shows the clinical result of this rehabilitation.

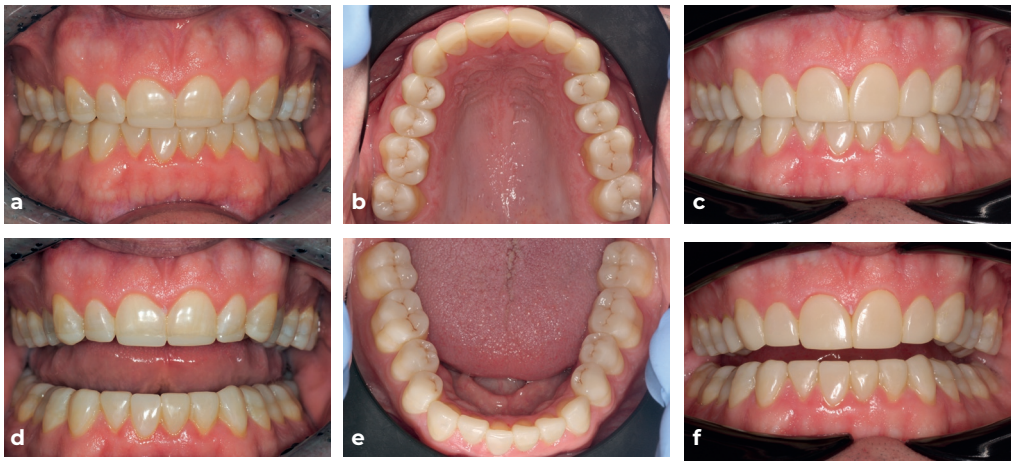

Figure 8: a) and d) before placement of buccal veneer restorations; b), c), e), f) after placement of buccal veneer restorations.

3 DISCUSSION

The aim of this case report was to describe the digital workflow that was applied for restoring a severely worn dentition with minimally invasive CAD/CAM resin nano ceramic restorations. After intake in our practice, the treatment plan for this patient could have been counseling and monitoring to evaluate the progression of tooth wear. The patient had, however, a demanded for treatment and it was decided to start restorative treatment. Identification of etiological factors is important to assess risk factors appropriately. However, this difficult and not always possible. Restorative treatment can be indicated in cases where tooth wear progresses rapidly or when severe clinical symptoms are present. There is no conclusive evidence that a specific treatment modality is favorable in terms of long-term clinical behavior for either chemical or mechanical tooth wear. Here, it was decided to use a restorative treatment modality that combined CAD/CAM technology with minimally invasive dentistry.

The goal of the treatment was to resolve functional problems and improve quality of life of the patient by reconstructing the anatomical form of teeth by functional thickness of restoration material. To restore lost tooth material, an increase of VDO was necessary by which the temporo-mandibular joint opened. The joint opens by rotation first, therefore the occlusal space for the posterior restorations was less than for the anterior restorations. Since anatomical form and VDO are no absolute, measurable clinical features, the new VDO in this procedure was established as a mixture of anticipated aesthetics and optimal posterior occlusal space as considered by the dentist (Fig. 3). To explore these features, we made a direct, free-hand mockup with composite in the mouth according to the lip-generated smile design [20], instead of the often-used temporary resin test build-up manufactured by the dental laboratory [7,16,19,21,22]. The latter approach, when supported by a digital smile design technique [23], is a formal method to achieve personalized aesthetics and can easily be transferred to the mouth by a mold. However, the digital 2D representation of aesthetics in a 3D model is still complicated, while the composite mockup technique reveals a direct visualization for the patient of the new intra-oral situation. Yet, the making of a direct mockup demands well developed operator skills as in a limited time frame an acceptable and for the patient pleasing result should be obtained. Finally, the presence of *e.g.*, an anterior open bite, an edge-to-edge incisor relationship, or an Angles Class II Division 1 occlusal relationship influences the determination of a new VDO. In those cases, an increase in VDO complicates achieving an appropriate anterior occlusal relationship or tooth length. Under such circumstances, the treatment plan may require amendments, such as a smaller increase in VDO, or switching to a multidisciplinary approach, including orthodontic treatment planning, to achieve a predictable treatment result.

According to a systematic review, raising the VDO is considered a safe and predictable treatment for patients without TMD or dysfunction problems [24]. The review showed that an increase of VDO up to 4 millimeters can be done without causing problems. In this case the new VDO was applied without a test-period and has not resulted in any complaints or interventions/adjustments. The patient was adapted to the new VDO within a week. It is described to include a period of adaptation to the increased VDO by a removable device like an acrylic splint [19]. There is anecdotal data that the splint will hardly be worn during the day due to oral and social discomfort. This decreases its effectivity as a means of try out. We therefore prefer to immediately increase VDO by fixed adhesive restorations, like others also have described [24-26]. It must be emphasized that a reluctant approach and use of a removable device is advised in patients that show signs of temporomandibular disorder.

In contradiction to functional dental rules, we did not provide the patient with a stable occlusion during the interim periods. The patient showed a good adaptability and overloading did not result in discomfort or pain. This type of trouble-free adaptation is also reported in papers describing the Dahl method, which promotes eruption of non-worn teeth by applying supraoccluding restorations to the worn teeth [27-29]. A complete rehabilitation of the dentition could be supported by the use of high-end occlusion and articulation registration instruments [30]. As we have a near complete digital fabrication procedure with a precise digital occlusion registration, we regard the scanning of the upper and lower dentition in centric relation using the bite blocks to be sufficient. Care was taken to have all restorations in static occlusal contact, including the anteriors. The active movements were guided by canine contacts to support posterior disclusion and by comfortable incisors contact. Moreover, the bite registration was done in the desired new VDO and therefore no adjustments in VDO were necessary in the dental laboratory.

In these complex rehabilitations a unity of restorative materials on all teeth can be preferred and we could have chosen to restore all teeth with direct resin composite restorations. It is reported that this type of direct treatment technique is quite commonly used for treating severe tooth wear [13]. However, building up posterior teeth with appropriate anatomical form and in adequate occlusal contact is strenuous and time-consuming. Indirect procedures, although costly, can be beneficial to obtain the required clinical quality in these cases. The CAD/CAM procedure that is used in this case study is simple and its treatment cost-effectiveness in comparison to that of direct restorations should be elucidated.

As the resin nano ceramic material was only available in blocks of one color, the buccal veneers were made of directly applied composite veneers using two color shades. With this type of resin material, we approached the unity of restorative materials on all teeth. If the patient would have had higher aesthetic demands, individually adapted (resin) ceramic veneers in the anterior area could have been an alternative. Cases with occluding composite restorations posteriorly and ceramic veneer restorations in the aesthetic zone have been described earlier and offer a fine compromise between occlusal adaptability and stable aesthetics [31].

The reason to place the buccal and palatal/lingual veneers in separate sessions, has to do with time constraints: it was not possible to treat all anterior teeth in one session. A critical point of this two-step treatment procedure for the anterior restorations is the bonding of the buccal veneer to the incisal edge of the palatal veneer. In severe wear patients that were restored with direct composite veneers on both the palatal/lingual and the buccal surfaces of anterior teeth, it was shown

that the incisal interface of the two veneers was significantly at risk of debonding when these two restorations were placed in separate treatment sessions compared to placement in one treatment session[9]. In this patient, we supported the adhesion by macro-mechanical and micro-mechanical roughening of the adhesive surfaces. In addition, silica coating with sandblasting and silanization were used prior to placement of the direct buccal veneer.

The veneer and tabletop restorations have minimal retentive capacity and intraoral occlusion check without the restorations being cemented was not possible. A positive finding was that the seating of the restorations was precise, and the occlusion did not require much finishing after placement. Since we had experienced those small discrepancies at the approximal areas of the restorations hampered the clinical seating of four tabletops in a row (*e.g.*, #34, 35, 36 and 37), we scanned and placed the posterior restorations in two separate procedures. Although this required at least one additional treatment session, the alternative, to adapt every single approximal surface before placing the restoration, would simply require even more time and efforts.

4 CONCLUSION

In the treatment of severe tooth wear, the described digital workflow using CAD/CAM resin nano ceramic for occluding restorations and direct composite materials in the aesthetic zone is a potential treatment modality that is workable and minimally invasive. The free-hand mockup technique to explore aesthetics and establish a new VDO was effective in this case.

5 ACKNOWLEDGEMENTS

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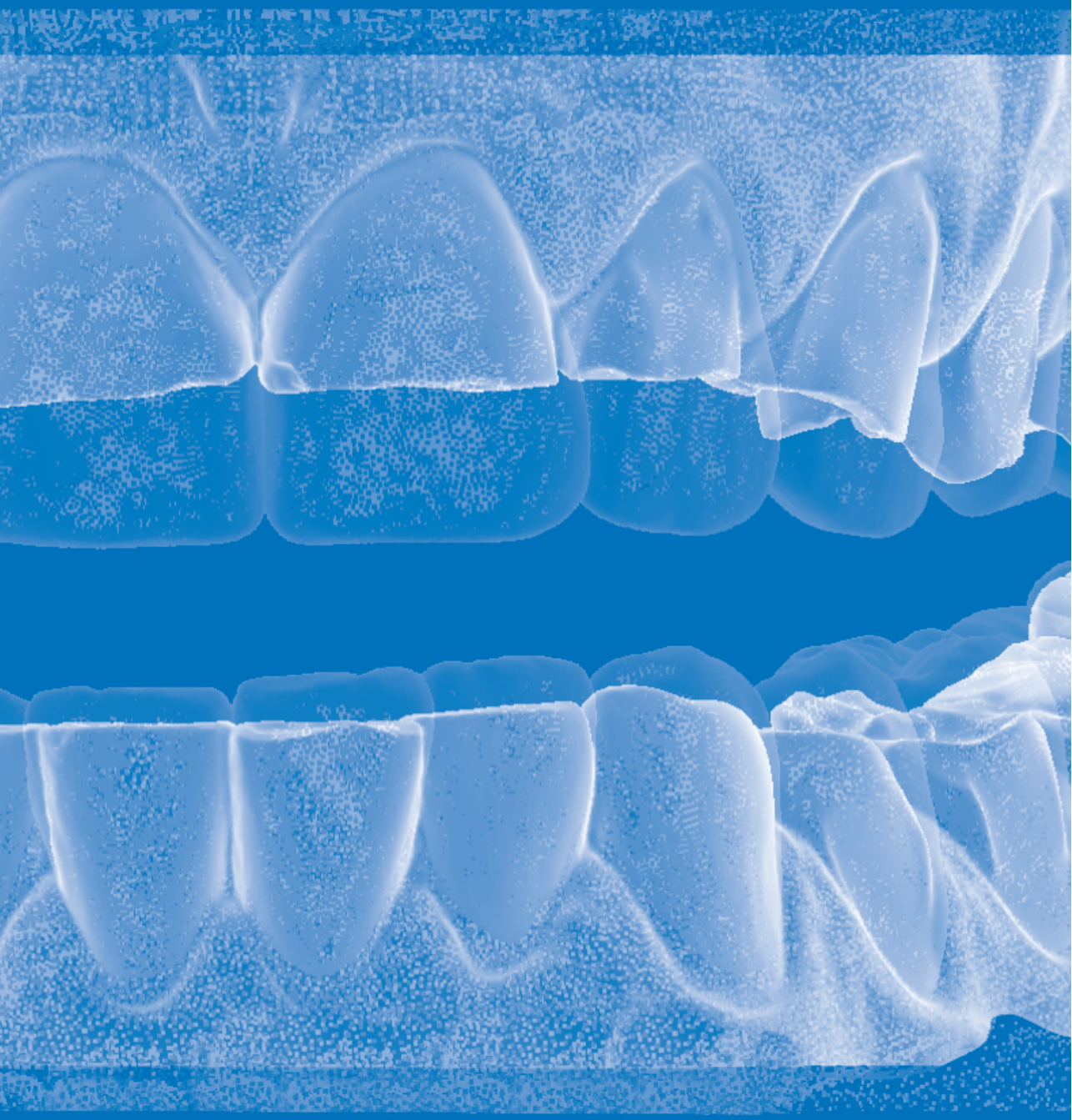

5

PROSPECTIVE STUDY ON CAD/CAM NANO-CERAMIC (COMPOSITE) RESTORATIONS IN THE TREATMENT OF SEVERE TOOTH WEAR

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ABSTRACT

Purpose: The aim of this prospective study was to evaluate the clinical performance of minimally invasive, CAD/CAM nano ceramic restorations in patients with severe tooth wear, to evaluate the effect of the restorative treatment on the Oral Health-Related Quality of Life (OHRQoL), and to evaluate the etiology of tooth wear as a risk factor for restoration failure.

Materials and Methods: Patients with generalized severe tooth wear were included. Restorations (LAVA Ultimate, 3M) were cemented (RelyX Ultimate, 3M) on all teeth and were evaluated after 1 month and 1 year. OHRQoL was assessed with questionnaires at baseline and after 1 year. Differences were evaluated (paired t-test). Two mechanical tooth wear lesions, that result of tooth-tooth-contact, and 3 chemical tooth wear lesions, that result of intrinsic or extrinsic acids dissolving natural hard tooth substance were evaluated to assess the etiology of tooth wear. Association with restoration failure was evaluated with multilevel logistic regression analyses ($p<0.05$)

Results: Twenty-one patients (age: 41.7 ± 10.4y) were evaluated after 1 year (13.5 ± 1.2m). 568 indirect CAD/CAM restorations were placed. None were replaced or lost. Twelve were repaired and ten were refurbished. Success percentages were 100% to 97.2%. Questionnaires showed a significant positive impact of the treatment on OHRQoL ($p<0.001$). Presence of mechanical lesions showed no higher risk for restoration failure ($p=0.78$). Presence of chemical lesions showed a lower risk ($p=0.002$).

Clinical Relevance: The use of minimally invasive, CAD/CAM nano ceramic restorations in the restorative treatment of severely worn dentitions showed satisfactory results in the short term.

1 INTRODUCTION

Tooth wear is a physiological process that may become pathological resulting in pain, masticatory dysfunction, severely impaired aesthetics, and loss of Oral Health-Related Quality of Life (OHRQoL) [1,2]. Restorative intervention is then a treatment strategy to regain function of the dentition [2] and to improve the OHRQoL [1]. Until now, there is no evidence regarding the best restorative intervention for severely worn dentitions, nor the restorative material [3].

The most commonly reported restorative treatment for worn dentitions is the placement of directly applied light-cured composite restorations on all teeth. This technique is particularly minimally invasive as no or very restricted preparation of tooth tissue is required. Favorable Annual Failure Rates (AFR) of about 2-3% using these restorations in load-bearing areas have been reported [4-7]. Less favorable AFR's (16% and higher) have also been reported indicating differences in success [8,9]. In patient centered care, outcome of restorative rehabilitation should also be evaluated from the perspective of OHRQoL, apart from the evaluation of restoration and material performance. The Oral Health Impact Profile (OHIP)[10], comprising specific subjective questions on diverse domains, and the Orofacial Aesthetic Scale (OES)[11], focusing on the aesthetic domain, have been used to assess the improvement of OHRQoL after restorative treatment of severe tooth wear [1,12], with positive results.

Reconstruction of the worn dentition is complicated as the procedure requires an increase of Occlusal Vertical Dimension (OVD). Although specific techniques [13-16] can be used to facilitate operators in shaping directly applied restorations, it remains complex.

This problem is avoided entirely when using indirect techniques, facilitating both shaping of restorations and obtaining the desired OVD. These techniques range from conventional impressions, which are used to construct restorations in a dental laboratory [17], to a complete digital workflow [18]. As adhesive dentistry has developed over the years, a shift in indirect techniques occurred from subtractive, invasive procedures with circumferential preparations [19] and (possibly) crown lengthening procedures [20], towards additive and conservative procedures [18,21], which are recommended in an European consensus statement [2].

Non-retentive indirect restorations on all teeth to restore worn dentitions have been described. Both lithium disilicate restorations, in a moderately invasive procedure [22], and CAD/CAM Polymer Infiltrated Ceramic Network (PICN), in a non-invasive (non-prep) procedure [21,23], showed good outcomes in the midterm

and short term, respectively. This suggests a place for additive indirect techniques in the restorative treatment of tooth wear, comprising minimally invasive CAD/CAM techniques. Composite and PICN materials, especially, offer advantages for the conservative management of tooth wear as they offer strong adhesive bonds and good repairability [24,25]. CAD/CAM techniques also offer superior materials properties such as lack of voids and higher degree of polymerization [26,27].

Severe tooth wear patients may constitute a high-risk population for restorative care. The etiological factors of tooth wear are likely still present after restorative treatment has been conducted, possibly impairing the longevity of the restorations [7]. In patients with mainly mechanical tooth wear, especially, more fractures of the restorative treatment are expected. Distinction between patients with mechanical and chemical tooth wear is difficult as the phenomenon of tooth wear is always multifactorial and scientific evidence is limited [28].

In the Radboud Tooth Wear Project, a group of patients with severe tooth wear was restoratively treated with minimally invasive CAD/CAM nano ceramic restorations, as described in a case report by Kreulen et al. The aim of this study was to evaluate the clinical performance of these restorations, to evaluate the effect of the restorative treatment on OHRQoL, and to evaluate the etiology of tooth wear as a risk factor for restoration failure.

2 MATERIALS AND METHODS

This study was a prospective clinical study evaluating the rehabilitation of tooth wear using minimally invasive CAD/CAM nano ceramic restorations (LAVA Ultimate, resin-nanoceramic material, 3M, Seefeld, Germany). The local medical ethics committee (CMO Arnhem-Nijmegen) confirmed that their approval was not required for this study (file nr. 2014-1252). Prior to commencement of the study, it was registered on ClinicalTrials.Gov (NCT02957734).

Patients with severe tooth wear were referred by their general dental practitioner to the RTWP at the Department of Dentistry of the Radboud university medical center in Nijmegen (The Netherlands). Inclusion was based on the following criteria: 1) Patients age ≥ 18 years; 2) Moderate to severe generalized tooth wear with functional problems and demand for treatment; 3) Full dental arches, although one missing tooth in the posterior area was allowed; 4) Required increase of OVD at first molars of at least 3mm. Exclusion criteria were (1) (history of) temporomandibular dysfunction, (2) advanced periodontitis (3) deep caries lesions;

(4) multiple endodontic problems; (5) local or systemic conditions that would contra-indicate dental procedures. Patients with specific individual risk factors, such as gastroesophageal reflux disease or parafunctional habits as grinding/clenching, were not excluded. All patients signed an informed consent document before entering the study.

At baseline, patients were asked to complete the OHIP-NL questionnaire [10,29,30] and the OES-NL questionnaire[11]. Patients completed both questionnaires after instruction. For each statement of the OHIP-NL questionnaire, patients were asked how frequently they experienced the impact of the specific statement. Higher scores imply a more impaired OHRQoL as answers were scored on a 5-point ordinal scale, ranging from never (1), hardly ever (2), occasionally (3), and fairly often (4), to very often (5). Three questions, exclusively referring to dentures (no 9, 18, 39), were omitted from the questionnaire.

The OES-NL questionnaire used an 11-point ordinal scale, ranging from very dissatisfied (0) to very satisfied (10). The questionnaire consisted of 8 items. Item 1 to 7 addressed the appearance of the face, profile, mouth, tooth alignment, tooth shape, tooth color, and gums. The last item (no. 8) characterizes the patient's overall assessment of orofacial aesthetics.

In addition, intra-oral examination, bitewing radiographs, a panoramic radiograph, and intra-oral photographs were collected for treatment planning and documentation. Intra-oral 3D scans (TrueDef, 3M) of the dentitions were made in maximum intercuspation. Deficient pre-existing composite restorations and all amalgam restorations were replaced using Filtek Supreme XTE (3M) and Scotchbond Universal (3M). The restorative status of abutment teeth at baseline, such as endodontic treatment and pre-existing restorations were registered on tooth-level.

Clinical presentation of tooth wear at baseline was scored using 3D-scans and intra oral images by one researcher (LC) on patient-level using an individualized index. This index was based on already existing indexes [28,31] and focused on 5 morphological features of tooth wear lesions.

Features of mechanical tooth wear:

1. A similar degree of wear in all occluding sextants[28]
2. The imprint of mandibular anterior teeth on palatal surfaces of maxillary anterior teeth

Features of chemical tooth wear:

1. Presence of 'raised restorations'[28]
2. Loss of convexities on the palatal surface of maxillary teeth[28]
3. Preserved enamel 'cuff' in the gingival palatal crevice of maxillary anterior teeth[28]

Patients received a score for both mechanical wear etiology, 0 to 2 depending on the numbers of features presented, and for chemical wear etiology, with scores from 0 to 3.

Restorative Procedure

Patients were assigned to one of 4 operators who were experienced and trained in adhesive dentistry and the specific protocol for placing indirect CAD/CAM restorations. To calibrate clinical procedures, multiple sessions were held before the onset of the study. Furthermore, pilot studies were performed to optimize the restorative protocol.

Increase of OVD

The increase of OVD was based on the space needed to lengthen the maxillary and mandibular anterior teeth and on the required interocclusal space of >1.5 mm for restorations' thickness in load-bearing areas. The estimated new OVD was determined intra-orally by applying a free-hand composite mockup on mandibular central incisors (Fig 1). A composite jig was made on palatal surfaces of the maxillary central incisors with the patient closing along the retruded path of closure [32] while there was an occlusal space between the (pre)molars. This new OVD was preserved by adding fast-setting, stiff polyvinylsiloxane silicon bite blocks (Star VPS, Danville Materials) at the right and left posterior areas, while the patient was in centric relation [32] closing on the anterior mockups." The mock-ups were documented using photographs and a 3D-scan after the patient's approval regarding the aesthetic aspects was obtained.

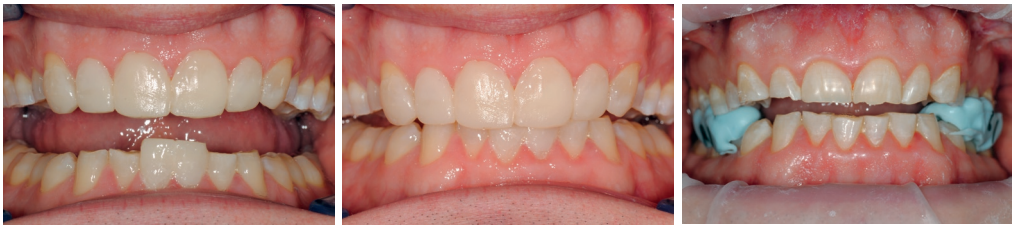

Figure 1: Mockups on the maxillary and mandibular anterior teeth and silicon stops *in situ* to preserve the new VDO.

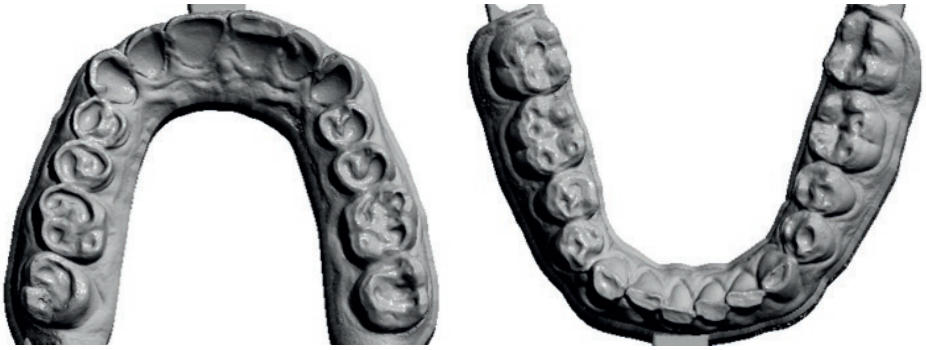

Figure 2: 3D scan after minimally invasive preparation.

Minimally invasive preparation

A minimally invasive tooth preparation was performed. It comprised removal of sharp edges and a shallow chamfer to determine the outline for the dental technician (Fig 2). In selected cases, and especially in lingual surfaces of anterior teeth, seats were prepared where otherwise no 'resistance' [32] of restorations could be obtained and seating of restorations could be enhanced. Intra-oral 3D-scans (True Def IOS, 3M) were made, including bite registration in the increased vertical dimension, while intra-oral stops were placed in situ to mimic the desired predetermined OVD.

Virtual wax-ups on digital models were made by the dental technician (Elysee Dental, Modern Dental Group, Alphen aan de Rijn, The Netherlands). After agreement of the operator, restorations were milled and finished. To avoid errors of seating during cementation, two series of planning, milling, and cementation of restorations were conducted. The first series was completed for all maxillary and mandibular anterior teeth (palatal/lingual veneer restorations), all second premolars, and all second molars. The second series was completed for all first premolars and first molars. No temporary restorations were placed before placement of the restorations, nor were they placed in between the two cementation sessions.

Cementation of CAD/CAM nano ceramic restorations

Rubberdam or cotton rolls and suction devices, at the discretion of the operator, were applied for moisture control. Teeth were cleaned using pumice and rinsed subsequently. LAVA Ultimate restorations were checked for their seating, and then cleaned and roughened using air-abrasion (30 µm, CoJet, 3M). Both a silane layer (ESPESIL, 3M) and an adhesive layer (Scotchbond Universal, 3M) were applied to the adhesive surface of the restoration. If a pre-existing restoration was present in the abutment tooth, it was air-abraded (CoJet). The tooth was etched for 15 sec using 37% phosphoric acid (3M) and rinsed for 10 sec. Silane was applied in case

of a pre-existing restoration in the adhesive surface. Next, the adhesive layer was applied on the tooth surface for 20 sec and polymerized for 15 sec. The restorations were cemented (RelyX Ultimate, 3M) and, after removal of cement excess, light-cured for 20 sec per restoration surface (Bluephase 16i, Ivoclar Vivadent; maximum output 1.600mW/cm^2). Occlusion and articulation were checked to ensure supported occlusion. Occasionally, small adjustments were made using fine grit diamond burs and polishing rubbers.

Facial veneers were made using directly applied composite (Filtek Supreme XTE, 3M) on all maxillary anterior teeth. In cases where LAVA Ultimate restorations were placed on lingual sides of mandibular anterior teeth, additional direct facial veneers were made (Fig 3). To ensure optimal adhesion between lingual/palatal indirect veneers and the facial veneers, the former was roughened with a bur and air-abraded, and silane was used as described above. The facial veneer was considered and evaluated as a separate restoration on the same tooth.

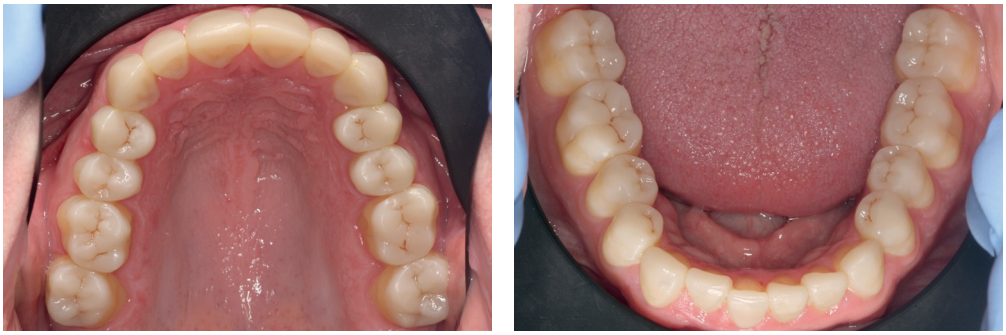

Figure 3: After placement of CAD/CAM nanoceramic restorations and facial veneer restorations.

Follow-up

Recall appointments were scheduled at 1 month and 1 year after treatment. Restorations were assessed (LC, BS, BL) using intra-oral examination, intra-oral photographs and 3D scans (TrueDef, 3M), focusing on functional (debond or fracture), biological (caries, endodontic treatment), and aesthetic criteria. Restorations with discoloration or roughness needing refurbishment by polishing were not considered as failures. Three levels of failure were distinguished:

F1. Restorations with severe deficiencies that were replaced or in case of an extracted abutment tooth

F2. Restorations with localized deficiencies, that were repaired or when a complete debonded restoration could be recemented (Fig 4a)

F3. Restorations with small material chippings (that received either refurbishment by polishing or needed no intervention) (Fig 4b)

Finally, the date of restoration placement, date of both check-up visits, and type and reason of failure were recorded. Patients completed both the OHIP-NL and OES-NL questionnaire at the recall appointment of 1 year.

Statistical analyses

Descriptive statistics were analyzed for all restorations. Success rates were calculated for indirect restorations and facial direct veneers separately, for different failure levels. Furthermore, the restorative status of abutment teeth (restored/endodontic treatment) were assessed as possible risk factors for the failure of the restorative treatment using descriptive statistics. Data of the questionnaires at baseline were compared with data after 1 year. The differences between the outcomes measured by questionnaires at the baseline and year 1, were analyzed using paired t-tests. This was feasible as a consequence of the normal distributions seen in these differences. Mean scores for the OHIP-NL questionnaire were calculated and compared between timepoints, as were summary scores (question no. 1 to 7) for OES-NL questionnaires. A separate analysis was completed for question no. 8 (Overall impression question). For analyzing the association of restoration failure (F1+F2+F3) with tooth wear etiology, multilevel logistic regression analyses, with a random intercept for patient were used. Separate analyses were completed for features of mechanical and chemical tooth wear lesions. The analyses were conducted within the R-software (v 3.6.2) and SPSS-software (v 25). The significance level was set for all tests at $p<0.05$.

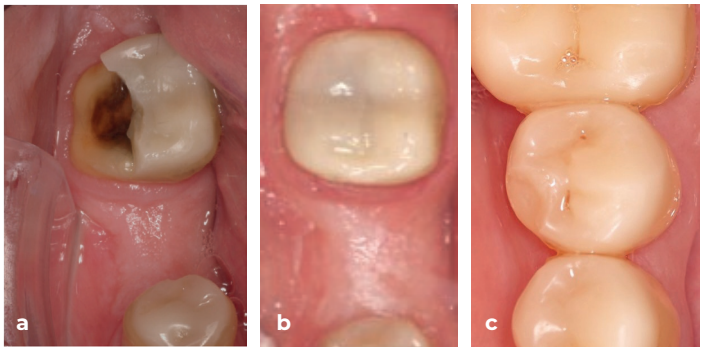

Figure 4: Adhesive fracture (a) and the repair (b) of a restoration on tooth #47; (c) Chip fracture of a restoration on tooth #35.

3 RESULTS

Inclusion of patients took place between February 2014 and January 2018. Twenty-two patients were treated using the treatment protocol, of whom 1 patient was lost to follow-up because of uncovered treatment costs (recall rate = 95%). Complete clinical follow-up was conducted for 21 patients (18 male; 3 female) with a mean age of 41.7 ± 10.4 y. The mean observation time was 13.5 ± 1.2 m (Fig 5).

In total, 768 restorations were placed in 21 patients, comprising 200 direct facial veneer restorations and 568 indirect restorations. Of these indirect restorations, 158 were placed on molars, 163 on premolars, and 247 on anterior teeth. In 10 cases, mandibular anterior teeth received indirect lingual veneer restorations. In 12 cases, mandibular anterior teeth received indirect facial veneer restorations. The mean increment of OVD measured at the first molars was 2.8 ± 0.7 mm (table 1).

During the observation time, 32 interventions were carried out, of which 22 were performed on indirect restorations and 10 on facial veneers. The main reason for intervention was fracture (31 out of 32). No indirect restorations were replaced or lost. Two indirect restorations debonded and could be recemented and were therefore regarded as a second level-failure (F2). Two facial veneers were replaced (table 2). Success percentages of indirect restorations were calculated. Depending on the 3 failure levels, success percentages were 100% (F1), 99.2% (F1+F2), and 97.2% (F1+F2+F3). Success percentages of direct veneer restorations were 98.3% (F1), 97.9% (F1+F2), and 96.5% (F1+F2+F3) (table 3).

Of the 568 restored teeth, 10 teeth had been endodontically treated at baseline. 1 indirect restoration placed on these teeth was repaired. 148 restorations were placed on an abutment tooth containing a pre-existing composite restoration in the adhesive surface. This subgroup of restorations consisted of 10 veneers with no interventions and 138 indirect restorations with 11 interventions (out of 32) (supplementary data).

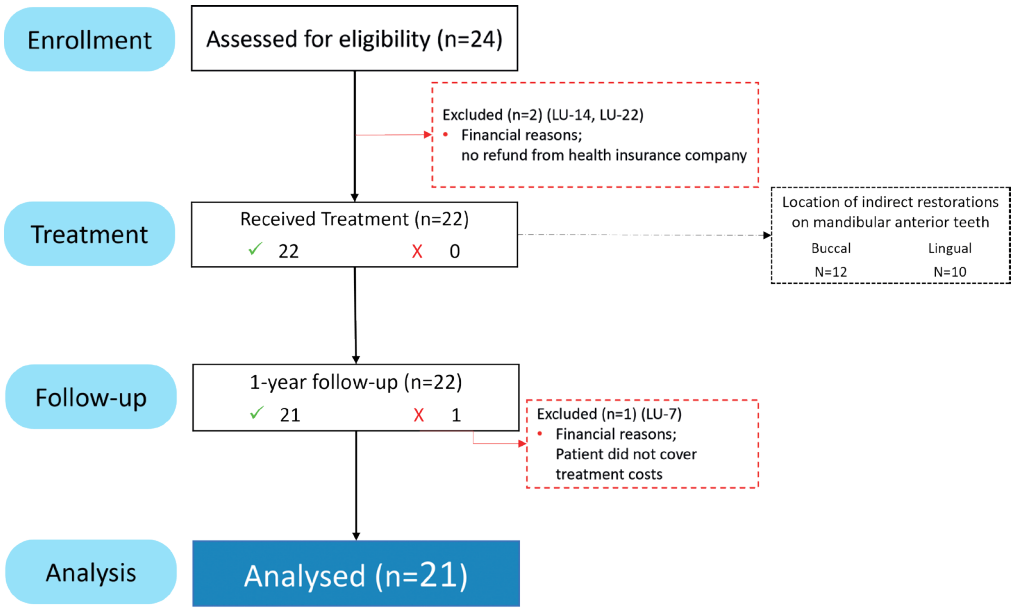

Figure 5: Flowchart of patients regarding allotted treatment, follow-up, and analysis.

Twenty patients completed the OHIP-NL questionnaire at baseline and after 1 year. After 1 year, the treatment resulted in a significant improvement of the OHRQoL as the questionnaire of the OHIIP-NL had a statistically significant lower mean score. A mean difference per question of -0.7 ± 0.5 (p<0.001) was found. Nineteen patients completed the OES-NL questionnaires at baseline and after 1 year. The aesthetic appearance also significantly improved as for both the summary score of questions no. 1 to 7 (average difference of 29.6 (p<0.001)) and the overall impression score (average change 3.7 (p<0.001), a significantly positive change was found. The changes in the OHRQoL are presented in table 4.

A first multilevel logistic regression analysis was conducted to check if presence of features of mechanical tooth wear at baseline were associated to a higher risk of restoration failure (table 5). The presence of 1 or 2 features, showed no significantly increased risk of restoration failure compared to the absence of these features (p=0.78; OR=7.4e^{7}; 95%CI=1.33-65.46). The analysis was repeated for the relation between the presence of features of chemical tooth wear and restoration failure. The presence of 2 or 3 features, compared to the absence of these features resulted in a significantly lower risk of failure, with a p-value of 0.002 (OR:0.03; 95%CI: 0.002-0.197) and 0.004 (OR: 0.15; 95%CI: 0.037-0.539), respectively.

Table 1 - Overview of patient characteristics, treatment specifics, and clinical outcome

Patient characteristics										Treatment specifics				clinical outcomes							
														F1: Replaced or lost		F2: Repaired		F3: Refur-bished		all	
Patient number	Patient ID	Sex	Similar degree of wear for all occluding sextants	Imprint of mandibular anterior teeth in maxillary anterior teeth	Loss of convexities on the palatal surface of maxillary teeth	Presence of 'raised restorations'	Enamel 'cuff' in gingival crevice of maxillary anterior teeth	# features of mechanical wear	# features of chemical wear	# Treated Teeth	VDO increment at location of first molar (mm)	Night-guard	Observation time (m)	Filtek Supreme XTE (n=200)	LAVA Ultimate (n=586)	Filtek Supreme XTE (n=200)	LAVA Ultimate (n=586)	Filtek Supreme XTE (n=200)	LAVA Ultimate (n=586)	All interventions	# interventions related to fracture
1	LU-1	m	1	1	0	0	0	2	0	25	2,9	yes	12.8	1					1	2	2
2	LU-2	m	0	0	1	1	1	0	3	26	1,7	yes	14.7								
3	LU-3	m	1	1	0	0	0	2	0	27	2,3	yes	13.5				3		5	8	8
4	LU-4	m	0	1	0	1	1	1	2	27	3.0	no	13.1								
5	LU-5	m	1	1	0	1	0	2	1	28	3.0	no	12.1			1	1		1	3	3
6	LU-6	m	1	0	1	1	1	1	3	28	3,2	no	13.2				1			1	1
7	LU-8	m	0	1	0	1	0	1	1	28	2,8	yes	14.8			2	1			3	3
8	LU-9	m	1	1	0	1	0	2	1	28	2,5	no	14.3			1	1			2	2
9	LU-10	f	0	1	0	1	0	1	1	28	3,3	no	12.9				1	2	2	5	5
10	LU-11	m	0	0	1	1	0	0	2	27	3,5	no	11.4								
11	LU-12	m	0	1	1	1	1	1	3	28	1,2	no	10.4				1			1	1
12	LU-13	m	0	1	0	0	0	1	0	28	3.0	no	14.0	1		2				3	2
13	LU-15	f	0	1	0	1	1	1	2	28	3,5	no	14.0								
14	LU-16	m	0	1	1	1	0	1	2	27	4,1	no	14.5								
15	LU-17	f	1	1	0	1	0	2	1	28	1,9	no	12.8				1			1	1
16	LU-18	m	1	0	1	1	0	1	2	28	2,9	no	15.8				1			1	1
17	LU-19	m	0	0	1	0	1	0	2	28	2,9	no	14.0								
18	LU-20	m	1	0	1	1	1	1	3	27	2.0	no	13.3								
19	LU-21	m	0	0	1	0	1	0	2	26	2,8	no	12.6								
20	LU-23	m	0	1	1	1	1	1	3	25	3,3	no	14.5				1			1	1
21	LU-24	m	1	0	1	1	1	1	3	28	3,4	no	13.8						1	1	1
MEAN		41.7								**27**	2.8		13.5								
SD		10.4								**1**	0.7		1.2								
TOTAL														**2**	**0**	**6**	**12**	**2**	**10**	**32**	**31**

Table 2 - Overview of interventions

		Interventions		
		F1: Replaced	F2: repaired	F3: Refurbished
Indirect restorations (n=568)	Complete debonding		2	
	Adhesive fracture		10	
	Chip fracture			10
	TOTAL	0	12	10
Direct restorations (n=200)	Bulk fracture	1		
	Adhesive fracture		6*	
	Chip fracture			2
	Aesthetics*	1*		
	TOTAL	2	6	2
TOTAL		2	18	12

*restoration was replaced after a repair due to fracture resulted in a poor aesthetic outcome

Table 3 – Success percentages

LAVA Ultimate restorations	Failure criteria	Group	No. of Failures	Success at 1-year recall (%)
n=568	F1	Whole group	0	100
	F1 + F2	Whole group	12	97.9
	F1 + F2 + F3	Whole group	22	96.1
Filtek Supreme XTE restorations				
n=200	F1	Whole group	2	99.0
	F1 + F2	Whole group	7	96.5
	F1 + F2 + F3	Whole group	9	95.5
Subgroup analyses of LAVA Ultimate restorations per location				
n=158	F1	Molar	0	100
	F1 + F2	Molar	7	95.6
	F1 + F2 + F3	Molar	13	91.8
n=163	F1	Premolar	0	100
	F1 + F2	Premolar	4	97.5
	F1 + F2 + F3	Premolar	7	95.7
n=247	F1	Incisors and canines	0	100
	F1 + F2	Incisors and canines	1	99.6
	F1 + F2 + F3	Incisors and canines	2	99.2

Table 4 – OHRQoL analyses: Comparison of baseline and 1-year OHIP mean score (± SD), OES summary score (± SD), and OES overall impression score (± SD)

	n	Mean at baseline	Mean after 1 year	Mean difference	95% CI of difference	p-value
OHIP mean score	20	2.0 (0.6)	1.3 (0.2)	0.7 (0.5)	0.4 - 1.0	<0.001
OES summary score (no. 1 to 7)	19	29.7 (9.9)	59.3 (5.2)	29.6 (12.9)	24.4 - 35.8	<0.001
OES no. 8 (overall impression)	19	4.8 (1.6)	8.5 (1.0)	3.7 (0.5)	2.7 - 4.7	<0.001

Table 5 – Multilevel logistic regression analyses for risk assessment of tooth wear phenotypes on restoration failure

All restorations in the prospective study (n=756)		N patients (total: n=21)	Interventions (F1+F2+F3) (total: N=31)	OR	p-value	95% CI of OR
Number of features of mechanical tooth wear at baseline	None (reference)	4	0	n.a.	-	-
	1	12	15	2.8 e+7	0.79	0.547-22.54
	2	5	16	7.4 e+7	0.78	1.33-65.46
Number of features of chemical tooth wear at baseline	None (reference)	3	12	n.a.	-	-
	1	5	14	0.61	0.32	0.212-1.84
	2	7	1	0.03	0.002	0.002-0.197
	3	6	4	0.15	0.004	0.037-0.539

4 DISCUSSION

The aim of this study was to evaluate the clinical performance of minimally invasive, CAD/CAM nano ceramic restorations in patients with severe tooth wear. Moreover, to evaluate the effect of the restorative treatment on OHRQoL and to evaluate the etiology of tooth wear as a risk factor for restoration failure. In the short term, success percentages between 100% and 97.2% were found with fracture as the main failure modality. This is comparable to an established treatment option for tooth wear; directly applied composite restorations [2,4-7,14]. Furthermore, the OHRQoL improved significantly. Such outcomes are not frequently reported related to the clinical performance of restorations but should be considered more often in the perspective of patient centered care. Although the follow-up of this trial is short, it can be assumed that the use of minimally invasive, indirect CAD/CAM restorations, without a retentive geometry, in the restorative treatment of tooth wear was successful after a period of 1 year.

Reporting about small material chippings as an outcome for the survival of restorations may be useful to demonstrate a tendency in studies with a limited observation time. The sensitivity of chipping can be material- and technique-specific and might be indicative for clinical behavior on the longer term. In addition, reporting about these outcomes is useful for optimal comparison with other studies. However, from the perspective of good care refurbished restorations are clinically acceptable and therefore arguably successful.

Despite the presence of bruxism and the non-retentive geometry of restorations, only 2 complete debonds occurred out of 568 tabletop LAVA Ultimate restorations, confirming its good adhesive ability. These findings are not congruent with the findings of a prospective study evaluating 50 LAVA Ultimate single crowns on zirconia abutments on dental implants with a retentive geometry, of which the survival was only 14% after 1 year [33] after multiple fractures and multiple debonds occurred. That study resulted in the manufacturer's retraction of the indication for LAVA Ultimate as a single crown material. As adhesive procedures were almost identical i.e., air-abrasion, silane application and the use of identical resin-cement, it seems likely that the substrate greatly influences the survival rate of the LAVA Ultimate restorations. This is supported by findings of another study that identified failure reasons for these particular single crowns on zirconia abutments, claiming the weakest link to be the adhesive layer between zirconia and resin-cement [34] and not the resin-cement-LAVA-Ultimate-interface. To assess the influence of the substrate on the survival rate of LAVA Ultimate restorations in this study, abutment teeth were checked for their restorative status as the presence of a composite restoration, that was sandblasted and treated with a silane in the present study, could be a risk factor for clinical failure. However, no signs or indications of a higher incidence of failure on restored teeth were found, within the limitation of the short observation time.

Patients suffering from severe tooth wear can be considered as high-risk patients that have a destructive oral environment that is likely to influence the longevity of restorations. While most patients only showed 0 or 1 interventions, 5 patients (patient nr 3,5,8,10,13) received 69% of all interventions (22 of 32) (see Supplementary data). Tooth wear is a multifactorial phenomenon involving both chemical and mechanical stress. We speculated that bruxism, related to mechanical stress, would be a risk factor for the survival of restorations [35] as frequent high masticatory forces may lead to early fracture of restorations. Meanwhile dental restorations potentially protect tooth tissues for chemical wear and therefore we speculated that patients suffering from chemical wear would be related to a superior longevity of restorations. To substantiate a clinical feeling on the etiology of tooth wear of the

patients, morphological features of tooth wear at baseline were scored. 5 features were selected of which 4 showed a significantly higher prevalence to either chemical (3 features) or mechanical (1 feature) tooth wear in a previous study [28]. An additional feature of mechanical tooth wear was scored as it can only be explained by mechanical stress, which is 'the imprint of mandibular anterior teeth in palatal surfaces of maxillary anterior teeth'.

Surprisingly, the presence of features of mechanical wear showed no significant higher Odds Ratio (OR) compared to the absence of these features. However, the presence of features of chemical wear, compared to absence, showed a statistically significant lower OR, indicating a lower risk of failure when features of chemical tooth wear were present. This might be explained by the fact that features of mechanical tooth wear are detectable in two situations: (1) patients with high mechanical stress and (2) patients with moderate mechanical stress in combination with chemical stress. In the latter situation, chemical stress leads to softening of hard tooth tissue making it vulnerable for tooth wear at low(er) mechanical stress [36,37].

Hence, in patients with severe tooth wear, features of chemical tooth wear may be discriminatory to distinguish between cases of high mechanical stress (in the absence of features of chemical tooth wear) and cases of mild to moderate mechanical stress (in the presence of features of chemical tooth wear). Within the limits of the present study, we therefore would consider the absence of features of chemical wear as a risk factor for restoration survival.

5 CLINICAL RELEVANCE

The use of minimally invasive, CAD/CAM nano ceramic restorations in the restorative treatment of severely worn dentitions showed satisfactory results in the short term. It seems that the absence of features of chemical wear in a patient with severe tooth wear indicates a higher risk for restoration failure.

6 ACKNOWLEDGEMENTS

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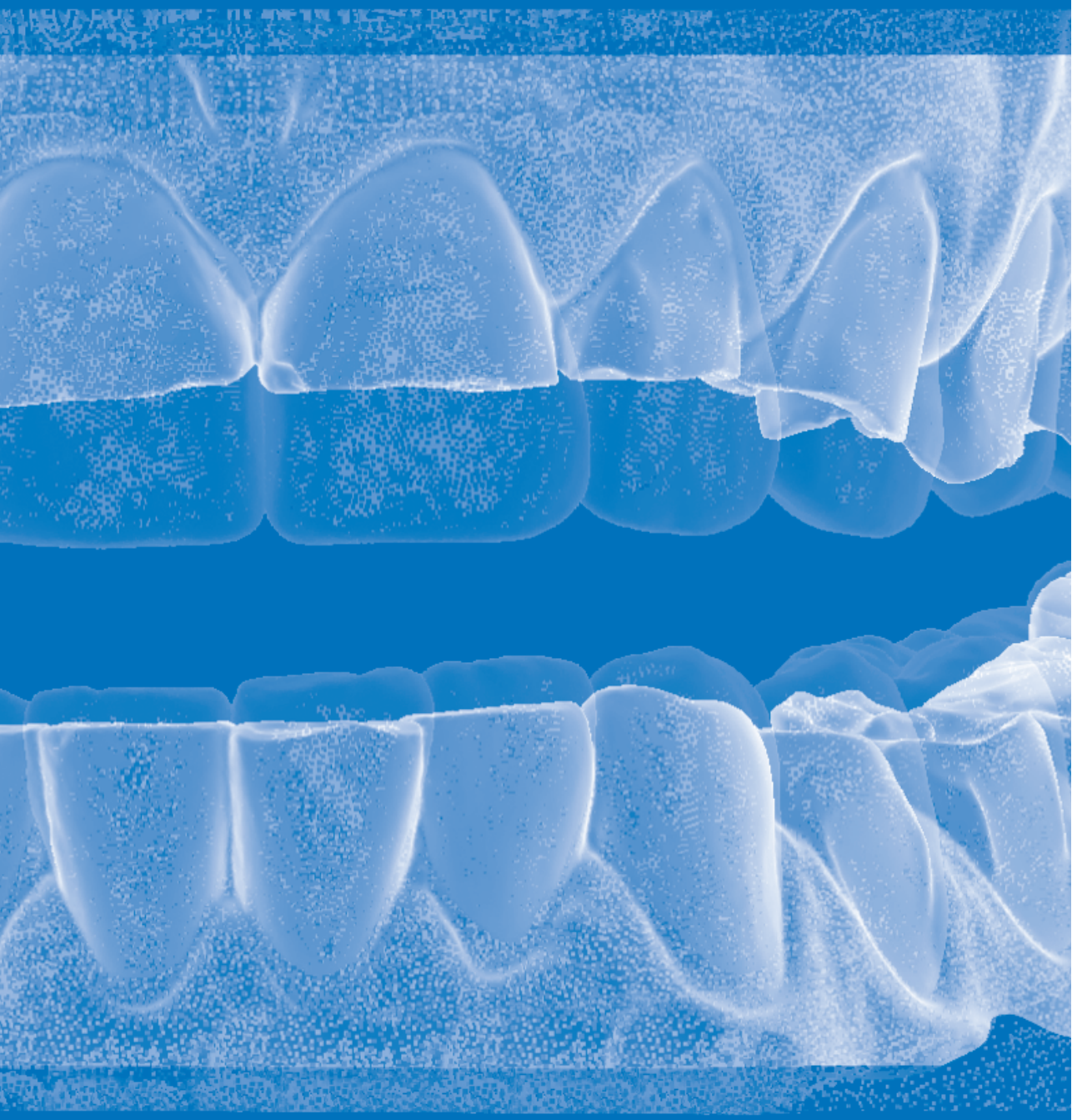
Supplementary Table – Overview of patient characteristics, restorations per location, and failures

Patient Charachteristics							Restorative Treatment														
							Overall			Filtek Supreme XTE			Lava Ultimate								
							All restorations			Buccal veneer			Anterior			Premolars			Molars		
Patient ID	Sex	Age (y)	Observation time (m)	# Treated Teeth	VDO increment (mm)	Night guard	# Restorations	# pre-existing restoration in adhesive suface	# endodontically treated teeth at baseline	# Filtek Supreme restorations	# pre-existing restoration in adhesive suface	# endodontically treated teeth at baseline	# Lava Ultimate anterior restorations	# pre-existing restoration in adhesive suface	# endodontically treated teeth at baseline	# Lava Ultimate anterior restorations	# pre-existing restoration in adhesive suface	# endodontically treated teeth at baseline	# Lava Ultimate anterior restorations	# pre-existing restoration in adhesive suface	# endodontically treated teeth at baseline
LU-1	m	66,3	12,8	25	2,9	Yes	40	21	0	15	4	0	11	5	0	8	6	0	6	6	0
LU-2	m	39,9	14,7	26	1,7	Yes	34	3	0	12	0	0	8	0	0	6	0	0	8	3	0
LU-3	m	39,4	13,5	27	2,3	Yes	33	7	0	6	0	0	12	0	0	8	1	0	7	6	0
LU-4	m	47,4	13,1	27	3,0	No	34	8	0	7	0	0	12	2	0	8	2	0	7	4	0
LU-5	m	45,4	12,1	28	3,0	No	40	9	0	12	3	0	12	2	0	8	2	0	8	2	0
LU-6	m	51,6	13,2	28	3,2	No	36	10	2	8	1	2	12	3	2	8	0	0	8	6	0
LU-8	m	29,0	14,8	28	2,8	Yes	40	5	1	12	0	1	12	1	1	8	1	0	8	3	0
LU-9	m	39,1	14,3	28	2,5	No	40	4	0	12	2	0	12	0	0	8	0	0	8	2	0
LU-10	v	42,5	12,9	28	3,3	No	40	12	0	12	0	0	12	0	0	8	4	0	8	8	0
LU-11	m	46,7	11,4	27	3,5	No	37	12	3	10	0	0	12	0	0	8	5	1	7	7	2
LU-12	m	22,5	10,4	28	1,2	No	40	0	0	12	0	0	12	0	0	8	0	0	8	0	0
LU-13	m	31,0	14,0	28	3,0	No	38	1	0	10	0	0	12	0	0	8	1	0	8	0	0
LU-15	v	28,6	14,0	28	3,5	No	40	3	0	12	0	0	12	0	0	8	0	0	8	3	0
LU-16	m	37,1	14,5	27	4,1	No	32	8	0	6	0	0	12	0	0	8	2	0	6	6	0
LU-17	v	30,6	12,8	28	1,9	No	42	2	2	14	0	0	12	0	0	8	0	0	8	2	2
LU-18	m	30,3	15,8	28	2,9	No	28	11	0	0	0	0	12	0	0	8	4	0	8	7	0
LU-19	m	39,7	14,0	28	2,9	No	36	2	0	8	0	0	12	0	0	8	0	0	8	2	0
LU-20	m	41,7	13,3	27	2,0	No	35	12	0	8	0	0	12	2	0	8	3	0	7	7	0
LU-21	m	40,5	12,6	26	2.8	No	32	5	1	6	0	0	12	0	0	6	0	0	8	5	1
LU-23	m	55,4	14,5	25	3,3	No	37	7	0	12	0	0	12	0	0	7	4	0	6	3	0
LU-24	m	24,9	13,8	28	3,4	No	34	6	1	6	0	1	12	1	1	8	1	0	8	4	0
Mean		41,7	13,5	27	2,8		37	7	0	10	0	0	12	1	0	8	2	0	8	4	0
SD		10,4	1,2	1	0,7		4	5	1	3	1	0	1	1	0	1	2	0	1	2	1
Total							768	148	10	200	10	4	247	16	4	163	36	1	158	86	5

Restorative Treatment				Clinical Observations																		
				Failures																		
Lava Ultimate				Filtek Supreme XTE				Lava Ultimate												Total		
Overall				Buccal veneers				Anterior teeth (I+C)				Premolar				Molar						
# Lava Ultimate anterior restorations	# pre-existing restoration in adhesive suface	# endodontically treated teeth at baseline		F1	F2	F3	Compromized substrate	F1	F2	F3	Compromized substrate	F1	F2	F3	Compromized substrate	F1	F2	F3	Compromized substrate	Failures	On compromised substrate	on endodontically treated teeth
25	17	0		1			*0*							1	*1*					2	1	
22	3	0																		0		
27	7	0											1	1	*1*		2	4	*5*	8	6	
27	8	0																		0		
28	6	0			1		*0*										1	1	*1*	3	1	
28	9	2															1		*0*	1		
28	5	1			2		*0*										1		*0*	3		
28	2	0			1		*0*		1		*0*									2		
28	12	0				2	*0*			1	*0*		1	1	*2*					5	2	
27	12	3																		0		
28	0	0											1		*0*					1		
28	1	0		1	2		*0*				-									3		
28	3	0																		0		
26	8	0																		0		
28	2	2															1		*1*	1	1	1
28	11	0															1		*1*	1	1	
28	2	0																		0		
27	12	0																		0		
26	5	1																		0		
25	7	0											1		*0*					1		
28	6	1																1	*0*	1		
27	7	0	Total	2	6	2	0	0	1	1	0	0	4	3	4	0	7	6	8	**32**	12	1
1	4	1	F1	2				0				0				0				2		
568	138	10	F2		6				1				4				7			18		
			F3			2				1				3				6		12		



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AN *IN VITRO* EVALUATION OF THE FATIGUE BEHAVIOR OF RESIN COMPOSITE MATERIALS AS PART OF A TRANSLATIONAL RESEARCH CYCLE

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In preparation

ABSTRACT

Purpose: This study aimed to reproduce and translate clinical presentations in an *in* vitro set-up and evaluate laboratory outcomes of mechanical properties (flexural strength, fatigue resistance, wear resistance) and link them to the clinical outcomes of the employed materials in the RTWP.

Materials and Methods: Four dental resin composites were selected. Thirty discs (Ø12.0 mm, 1.2 mm thick) were fabricated of Clearfil ™ AP-X (AP), Filtek ™ Supreme XTE (FS), Estenia ™ C&B (ES), and Lava Ultimate (LU). Cyclic loading (200N, 2Hz frequency, was applied concentrically to 15 specimens per group with a spherical steatite indenter (r=3.18mm) in water in a contact-load-slide-and-back motion (10^5 cycles). The wear scar was analysed using profilometry and virtual computation of the volume. All specimens were loaded until fracture in a biaxial flexural strength set-up. The volume of the wear scar was analysed in a regression analysis. The differences in flexural strength were analysed using a regression analysis with the material and the fatigue test as a variable.

Results: Compared to AP, ES and LU showed a significantly lower volume loss ($p=0.05$, 95%CI:-0.16 – 0.00). FS had a similar degree of volume loss. Non-fatigued ES specimens had a similar flexural strength compared to non-fatigued AP, while non-fatigued FS and LU specimens had a lower flexural strength ($p<0.001$; 95%CI: -80.0 – 51.8). The fatigue had a significant impact on the flexural strength of ES specimens, only ($p<0.001$; 95%CI: -96.1 – -54.6).

Clinical Relevance: These outcomes concur with the outcomes of clinical studies on the longevity of specific composite products in patients with tooth wear. The employed laboratory test can be regarded as clinically relevant as clinical presentations were emulated in the laboratory. Moreover, the first step in the translational research cycle has been made with the emulation of clinical presentations in the laboratory; 'from the clinic to the lab'.

1 INTRODUCTION

Tooth wear is a physiological process that, depending on the extent and rate of wear, may become pathological[1]. Especially in the context of less caries among younger people and a growing elderly population retaining their natural teeth, restorative treatment of tooth wear may be indicated more often. In case of a full rehabilitation of patients with severe tooth wear, minimally invasive restorative procedures are preferred that preserve the worn teeth and add restorative material without or with very limited preparation. This is a challenging restorative procedure as adhesive restorations in an increased vertical dimension of occlusion are required [1]. In those cases, the complete occlusal load is born by the restorative material and, as tooth wear patients are a high-risk group for parafunctional activities, these materials are challenged to their limits on fracture strength and wear resistance.

The Radboud Tooth Wear Project (RTWP) [2] focuses on the clinical management of patients with advanced stages of tooth wear. Within this project, multiple prospective clinical trials are embedded. A large group of patients (approximately 140) with generalized, moderate to severe, tooth wear was restoratively treated with direct and indirect composite materials as well as CAD/CAM composites [3-8]. The prospective studies evaluating direct composite restorations showed acceptable clinical success [3,5]. Whenever the clinical success was hampered, fracture of restoration was the main failure modality, with chip fractures occurring the most frequently within the observation period [3-5]. Although it was not a clinical concern within the observation time, wear of the materials could limit the survival of these composite restorations, on the long term. Comparing the wear for the two composite materials that were used in two prospective (hybrid and nanocomposite), no differences were observed[7,8]. A striking difference in clinical success was observed when directly comparing direct composite on molar teeth compared to indirect composite [3]. In that randomized controlled trial, material fracture was again the main failure modality, and it was concluded that the indirect composite was not suitable for restoring worn molar teeth. However, another prospective study in the RTWP showed similar failure rates for CAD/CAM indirect composite restorations as that was found for directly applied composite restorations. This suggests that the application technique itself is not necessarily causing higher risks for restoration failure. One of the reasons for the poor clinical result of the conventional indirect composite restorations on molar teeth is the individual susceptibility to fatigue or failure of a composite material. In vitro studies can help to understand specific clinical outcomes.

The classical direction of evaluating the performance of dental materials is to initially perform laboratory studies aiming to anticipate *in vivo* results prior to

undertaking clinical trials. Research aimed at converting results in basic research into results that directly benefit humans is often called translational research and can be described as "from lab to clinic". Unfortunately, in vitro tests struggle with their clinical relevance[9-11]. To improve the 'clinical value' of laboratory tests, information from the clinic should be incorporated into the laboratory set-up. The first possible step is to emulate clinical presentations in laboratory set-ups. When successfully emulated, modifications to laboratory set-ups may be introduced to allow for better preclinical testing of restorative materials and techniques that can benefit in vivo outcomes. These steps together can be repeated endlessly in a cycle best characterized as "from the clinic to the lab, and then back to the clinic".

From the perspective of the RTWP a better understanding of the materials' strength and wear resistance is needed. The clinical relevance of simple tests looking only at fracture strength or simulated wear, however, is not clear [9]. Fatigue testing is a time-challenging procedure but may be the most appropriate *in vitro* test for testing materials that are used for tooth wear rehabilitations (ref Wendler fatigue). Many *in vitro* methods for testing of dental materials use loading and wear simulation devices and present variations in chewing simulation mechanisms. Some devices apply mechanical cyclic compressive loads, with or without sliding. A method that has been shown to produce fatigue failures similar to those found clinically in tabletop ceramic restorations [12] applied mechanical compressive loads without sliding but did not show levels of (contact) wear. Static repetitive compressive loads may be assumed not suitable to reproduce the clinical presentation of restoration fracture and restoration wear as found in tooth wear patients. Other simulators, such as the Rub&Roll device [13], apply loads in a rolling motion in an endeavour to resemble chewing cycles. Recently, it was shown that the device was capable to produce deterioration compatible to erosive cup-shaped lesions([14] and to emulate the surface deterioration effects observed in composite restorations placed in patients with severe tooth wear [15]. Another recent study showed that repetitive impact-sliding movements allow for wear development and material fatigue at a lower number of cyclic loading [16] because it introduces superficial damage in some materials and it institutes friction between the indenter and substrate promoting a more dynamic stress distribution into the material.

To better understand the materials' effect on clinical performance of the restorations in the RTWP, this study aimed to reproduce and translate clinical presentations in an in vitro set-up and evaluate laboratory outcomes of mechanical properties (flexural strength, fatigue resistance, and wear resistance) and link them to the clinical outcomes of the employed materials in the RTWP.

2 MATERIALS AND METHODS

Materials

In this study, dental resin composites were used, which were also clinically used in the RTWP for the treatment of patients with moderate to severe tooth wear [3-8]. Two composites for direct application (Clearfil ™ AP-X, Kuraray (AP) and Filtek ™ Supreme XTE, 3M (FS)) and two composites for indirect application (Estenia ™ C&B, Kuraray (ES) and Lava Ultimate, 3M (LU)). Two subtypes of resin composite were included as AP + ES are micro-hybrid composites and FS + LU are nanocomposites. The used composite materials including abbreviations and compositions are listed in Table 1. A list of all materials and instruments used in this study can be found in the supplementary Table. The study included four composite materials that had both a control group and a test group. Only in the test group, a fatigue test was applied by mechanical cyclic loading. The number of specimens per group was set at 15.

Fabrication of specimens

Direct resin composites

A cylindrical defect with a diameter of 12.0 mm was created in a high-density polyethylene plate of 1.2 mm thickness, see Fig 1. This resulted in an individualized mould with dimensions of 12.0 by 1.2 mm (diameter x height). The mould was placed on a flat glass plate and the defect was compacted in bulk with AP and FS, respectively. Then, a second glass plate was placed on top and pressed onto the uncured composite. Light curing was performed through the glass plates using a polymerization unit (Bluephase 16i, Ivoclar (average output 1200mW/cm^2)) for 20 seconds from the upper surface and 20 seconds from the lower surface. The manufacturing process resulted in disc-shaped specimens that were later manually polished using 800-grit wetted sandpaper on both sides to mimic clinical polishing with fine-grit diamond burs.

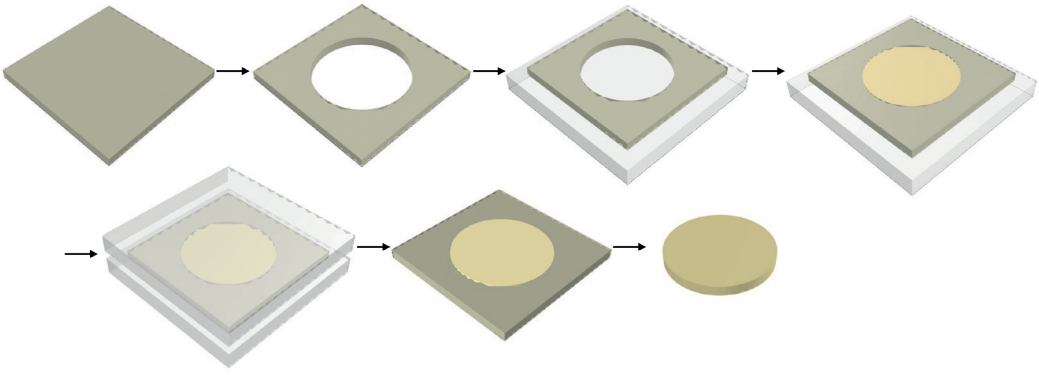

Figure 1: Schematic presentation of the production of direct resin composite discs

Indirect resin composites

The specimens of ES were fabricated using the same mould and application and polishing procedure as the direct composites. The difference with the direct composite specimens was that ES specimens received an additional 270 seconds (310 sec in total) of light curing from the upper surface and were also heat-cured in an oven (110° C, 15 min).

Pre-polymerized blocks of LAVA Ultimate (LU) were milled into cylinders with a diameter of 12.0 mm using a milling machine (CEREC Primemill, Dentsply Sirona). These cylinders were sectioned into discs with a thickness of 1.2 mm using a diamond blade with water-cooling in a universal cutting machine, see Fig 2. Polishing was performed identically to the other groups.

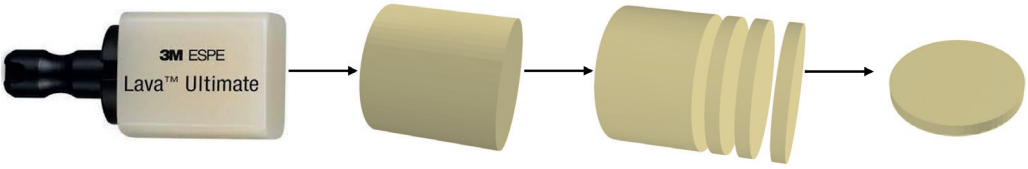

Figure 2: Schematic presentation of the production of composite discs out of prepolymerized blocks.

Fatigue test by cyclic loading

Specimens in the four test groups were cemented using Multilink® Automix (Ivoclar) onto previously hydrated (30 days storage in distilled water) fiber glass-reinforced epoxy resin (G10, Acculam, Yonkers), a dentin-analogous material [17]. G10 substrates were randomly chosen, and the adhesive surface was airdried for 60 sec. Then, Monobond Plus (Ivoclar) was applied to the surface with a microbrush and was left to react for 60 sec. The surface was subsequently dried with a stream of air. The disc-shaped specimens were cleaned in an ultrasonic bath with ethanol for 5 min and then dried using an air stream. The adhesive surface was cleaned with 4.5% hydrofluoric acid (IPS. Ceramic Etching Gel, Vita Zahnfabrik)) for 20 sec, rinsed with air/water spray, and dried with air. A silane coupling agent (Monobond Plus, Ivoclar) was applied to the surface with a microbrush and left to react for 60 sec. The specimens were cemented, using Multilink Automix (Ivoclar). Light curing of the luting agent was carried out by a LED curing light with an irradiance of 850 W/cm^2 for 40 sec for 4 consecutive times from different directions (Ultra Lume LED 5, Ultradent). After cementation, the specimen-G10 assemblies were stored in distilled water at 37C for 7 days for hydration. For reasons of standardization, specimens of the control group were also stored in distilled water at 37°C for 7 days.

The mechanical fatigue test was performed in a mouth-motion simulator (ELF-3300, EnduraTEC Division of TA Instrument). The specimens-G10 assemblies were placed onto an inclined block (θ = 30°) to generate off-axis loading of the indenter. The vertical loading of a spherical steatite indenter (radius 3 mm) resulted in an initial contact of the indenter with the specimen's surface at which the maximum load was transferred while sliding down (for about 1mm). After the maximum load, which was set at 200 N, was reached, the load was reduced, and the indenter slid back over the specimen's surface until it returned to its original position. The cycle can be described by contact-load-slide-and-back motion, as depicted in Figure 3. Specimens were subjected to 10^5 cycles of loading with a frequency of 2 Hz. The fatigue test was performed in distilled water.

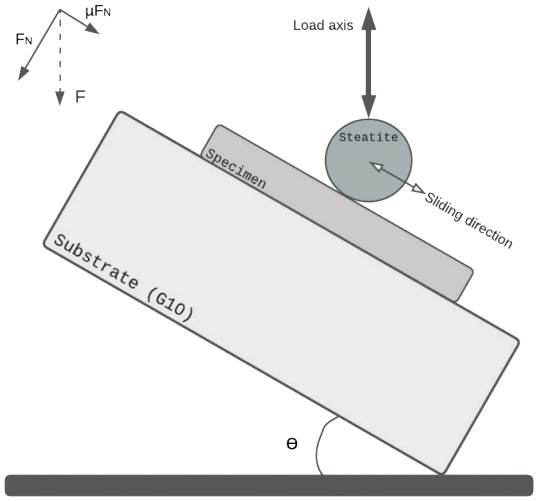

Figure 3: Schematic presentation of the loading configuration used in the study. The specimen was cemented onto a substrate and subjected to cyclic indentation with a spherical steatite indenter. A 30° inclination was used to facilitate a sliding motion of the indenter over the specimens' surface. The indenter slides over the specimens' surface for about 1 mm in the cyclic indentation.

Wear quantification

After the mechanical fatigue test, 7 specimens per group were inspected on wear using a non-contact Laser Abrasion measurement System (LAS-20, SD Mechatronik GmbH, Feldkirchen-Westerham, Germany) which does not require a stone replica or surface treatment of the specimen. The resolution was set at 0.001 mm. The scanned data was saved as a point cloud in an STL file and transferred to Geomagic Wrap Software (v 2017). Within this software, noise and spikes in the point clouds were removed by the function 'reduce noise' and 'remove spikes'. Additionally, small

'holes' in the point cloud were filled in by the software using the function 'mesh doctor'. The next step was to introduce a plane (function plane shape) and position it parallel to the specimen's unworn surface using the best-fit function. Subsequently, the edges of the wear scar were selected, and the polygon was trimmed to these edges. That resulted in the removal of the unworn surface adjacent to the wear scar. The selected edges of the wear scar were extruded (by 0.1 mm), using the function 'extruded boundary', with the goal to create a 'watertight' 3D volume. Then, this 3D volume and the reference plane were combined in which the reference plane acted as a cut-off. With the function 'Boolean; subtract', a 3D volume between the reference plane and the scanned surface of the wear scar could be realized. With the software function 'compute volume' the volume (μm^3) of the wear scar was assessed.

Flexural strength test

After being subjected to the mechanical fatigue test, and for some specimens also wear quantification, the G10 substrate of specimen-G10 assemblies was carefully cut, leaving a thin layer of G10 attached to the composite disc. The residual G10 could then carefully be removed by polishing the cementation surface of specimens using wetted sandpaper (grit 800). After polishing, the thickness of the composite specimens was measured.

A universal mechanical testing machine (model 5566; Instron, Norwood MA, USA), using a load cell capable of measuring applied loads of between 10 N and 1000 N (± 0.1 N), was used. The crosshead speed was set at 0.5 mm/min. A software program (Bluehill LE for Basic Testing, Instron) controlled the testing machine. Specimens were mounted in a piston-on-three-balls set-up (P3B-test) (ISO:6872), see Figure 4. Three hardened steel balls with a diameter of 3.17 mm, were positioned 120° apart on a support circle with a diameter of 8.0 mm. Specimens were placed concentrically on these support balls with fatigued specimens having the wear facet on the flexural side and not on the compressive side. The load was applied with a flat punch with a diameter of 1.37 mm at the center of the specimen, see Figure 5. All specimens were subjected to a single load to failure test. The maximum load at the moment of fracture was noted. The fracture was defined as a sudden drop of 40% of the load. Fragments of fractured specimens were collected and evaluated by stereo-light microscopy.

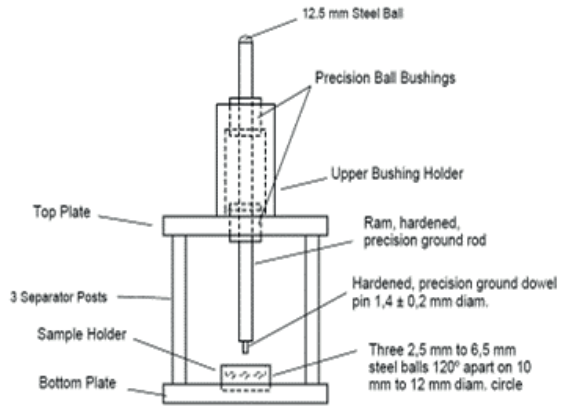

Figure 4: Schematic presentation of a fixture for the piston-on-three-ball test

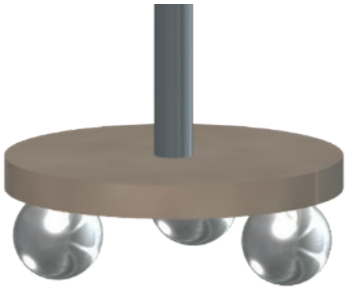

Figure 5: Schematic presentation of a composite disc in the P3B-test

Statistical analysis

Residuals in the data were checked. The volume of the wear scar after completion of the fatigue test was analysed in a regression analysis with the material as a variable. The differences in flexural strength were analysed using a regression analysis with both the material and the fatigue test as a variable. Also, the interaction between the material and the fatigue test was checked in the regression analysis. Differences between materials were displayed in graphs showing the 95%CI of the mean values of both wear volume and flexural strength. R-software (v 4.1.3) was used to perform the analyses.

3 RESULTS

Results for the wear volume of the four composite materials are graphically displayed in Figure 6. Wear scars could be observed in all specimens that were subjected to the fatigue test. Typical examples of wear scars per material are displayed in Figure 7. The mean volume loss of material was 0.25 ± 0.09 mm^3 for AP, 0.26 ± 0.08 mm^3 for FS, 0.17 ± 0.05 mm^3 for ES, and 0.16 ± 0.04 mm^3 for LU. With AP as a reference group, FS showed a similar degree of volume loss, but both the indirect composites had significantly lower volume loss, see Table 2.

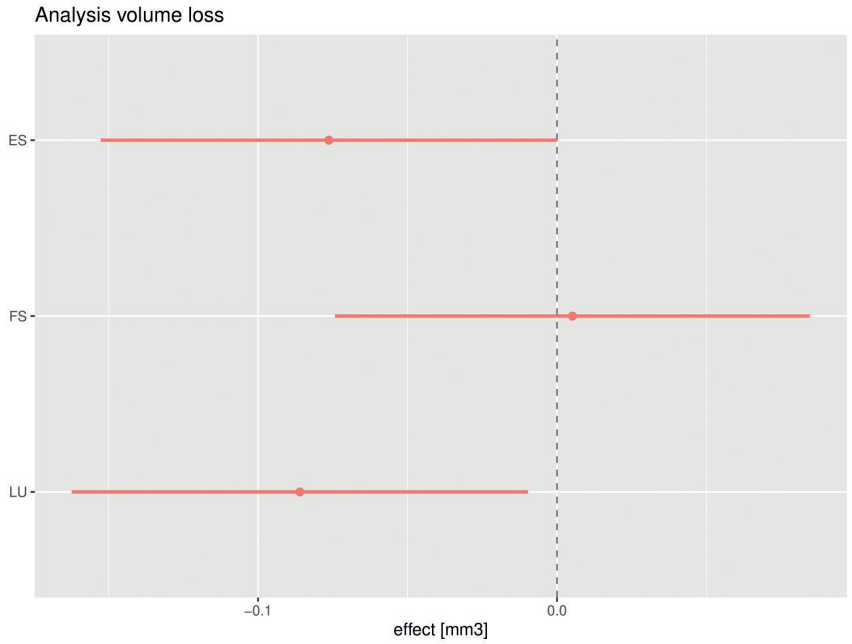

Figure 7: SEM images of examples of a worn surface the specimens. In the center of the images, an oval wear scar can be observed. These wear scars are a result of repeated contact-load-slide-and-back motion (A: AP, B: FS, C: ES, D: LU).

The flexural strength of the composite discs was analysed for the effect of the material, the effect of the fatigue test and the interaction between the material and the fatigue test. The 95%CI of the mean values can be found in Figure 8, in which non-fatigued AP was used as the reference group. Non-fatigued ES showed similar flexural strength (p=0.65; 95%CI: -10.9 – 17.4). Both non-fatigued nanocomposites (FS + LU) had a significantly lower flexural strength compared to AP (p<0.001; 95%CI: -80.0 – 51.8), see Figure 7. The fatigue test had no significant effect on the flexural strength of AP-specimens (p=0.19; 95%CI: -24.5 – 4.8). No significant effect of the interaction between the fatigue test and the material could be observed for

FS and LU specimens (p>0.09; -10.7 – 38.8). However, the interaction between the fatigue tests and the ES composite had a significantly negative effect on the flexural strength (p<0.001; 95%CI: -96.1 – -54.6). During the mechanical fatigue test phase, no catastrophic failures occurred.

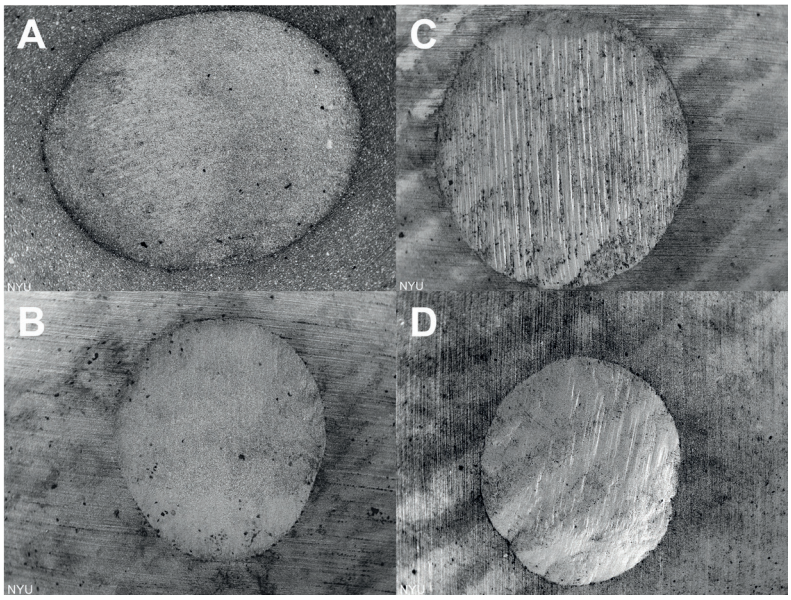

Figure 8: Graph of the 95% CI of the flexural strength of the regression analysis. The dotted line on effect 0 N is the reference group which is non-fatigued AP. The 'Fatigue' is the effect of the fatigue test on the flexural strength of the AP specimens.

4 DISCUSSION

This study aimed to reproduce and translate clinical presentations in an *in* vitro set-up, evaluate laboratory outcomes of mechanical properties (flexural strength, fatigue resistance, and wear resistance) and link them to the clinical outcomes of the employed materials in the RTWP. The main outcomes of this study were the higher initial biaxial flexural strength of hybrid composites (AP and ES) compared to the nanocomposites FS and LU. In addition, the biaxial flexural strength of mechanically fatigued specimens was similar to the initial biaxial flexural fracture strength for AP, FS, and LU. ES specimens, however, showed a significantly lower biaxial flexural strength for the fatigued specimens compared to the non-fatigued specimens. Also, the direct composites (AP+FS) showed higher levels of volumetric loss due to the wearing-away in the fatigue test compared to the indirect composites

(ES+LU). An interesting observation in this study is that fatigued specimens of AP, FS, and LU, that had a wear scar because of the fatigue test, had similar biaxial flexural strengths as non-fatigued specimens. The loss of restorative material seemed to have no negative effect on the biaxial flexural strength of the specimens.

One of the trials within the RTWP, evaluating the clinical success of directly applied composite (AP) and indirectly applied composite (ES), showed a poor clinical success of ES-restorations when used on molar teeth. Restoration fracture was the main reason for failure. One of the reasons for the differences in the clinical success of these materials could be the application technique. However, another study within the RTWP evaluating the clinical success of indirect CAD/CAM restorations (LU), showed a level of restoration failure similar to directly applied composite restorations (AP). This suggests that other factors than the application technique are involved in the higher failure rates of ES and that the mechanical properties of the specific materials may be contributing to the outcomes. Combining the outcomes of the studies within the RTWP it may be roughly concluded that restoration fracture is the most important reason for failure on the short term when restoratively treating tooth wear[3-5]. However, on the long-term wear of restorative material may limit clinical success. The *in vivo* wear of micro-hybrid (AP) and nanocomposite (FS) restorations showed similar levels after 5 years of clinical service [7]. This indicates that, for directly applied composite, the subtype of composite does not affect the wear rate *in vivo.* No such clinical data is available for the indirect composites within the RTWP. Some of the findings within the present study are therefore congruent with the clinical outcomes. The poor clinical success of ES-restorations may be explained by a lower fatigue resistance of the material that was found in this study. In addition, the similar levels of occlusal (contact) wear for direct micro-hybrid and nanocomposites *in vivo,* were congruent with the findings of the present study. With the emulation of clinical presentations in the laboratory, a successful first stap has been made in the translational research cycle; 'from the clinic to the lab'.

Table 1 presents an overview of the characteristics of the tested composite materials. It includes details about their composition and mechanical properties. FS and LU are both nanocomposites and have similar organic and inorganic components with similar filler contents (73/56 and 80/65 (w/v)). AP and ES are micro-hybrid composites with high inorganic filler content (86/70 and 92/82 (w/v)) and higher Young's moduli. The biaxial flexural strength of non-fatigued specimens was significantly higher for the hybrid composites compared to the nanocomposites. Higher filler percentages of composites contribute to higher flexural strengths [18,19]. FS and LU are nanocomposites containing similar nanoclusters of silica fillers (20nm) and zirconia fillers (4-11nm) nanoclusters as filler particles and have lower filler

content and lower Young's moduli compared to the hybrid composites. Zirconia has a higher hardness value than the other substances in the composite materials and steatite [20]. When the load-slide-and-back motion is repeatedly performed, particles of zirconia may have dislodged. These dislodged particles may then have scratched the surface of the specimens as a form of abrasive wear. That may be a reason why scratches can be seen on the surface of the wear scar for FS and LU (see Fig 7).

The tested materials can be considered direct-indirect pairs of both micro-hybrid and nanocomposites. LU is delivered in industrially manufactured blocks, and ES, although it is delivered in unpolymerized form, comparable to a direct resin composite, is processed additionally with light curing and heat curing to increase mechanical properties. Keeping the similarities in mind, ES and LU may be roughly regarded as versions of respectively AP and FS with (expected) improved mechanical properties. Therefore, we would expect better outcomes on fracture strength, fatigue resistance, and wear resistance for these indirect composites compared to their 'direct' variant. Higher biaxial flexural strength of the CAD/CAM nanocomposite (LU) for both fatigued specimens and control specimens compared to the 'direct' variant (FS) was observed. Also, superior wear resistance was observed for LU compared to FS. This was, however, not significantly different, likely because of a lack of statistical power. The manufactured blocks (LU) offer better mechanical properties than the direct variant (FS). The industrial process to manufacture the prepolymerized blocks may lead to increased mechanical properties due to maximum control of the quality and homogeneity of the material. In contrast, no beneficial effect of the indirect processing (additional light curing and heat curing) on the mechanical properties could be observed for ES, when compared to its 'direct' variant. Similar flexural strength was found when no fatigue test was performed. Surprisingly, a significantly lower flexural strength for fatigued ES was observed while no lower flexural strength was observed for fatigued AP. Moreover, the lowest fracture resistance after cyclic loading was found for ES of all four materials. The reason for this is unknown, but some explanations may be explored. Firstly, porosities may lead to stress concentrations and increased fatigue, but it is hard to argue this would play a larger role for this material than for the two direct composites. Also, no such porosities could be observed at the fracture surfaces of the fragments of fractured specimens (with stereomicroscope and fractography). Secondly, the additional curing of ES may cause it to become brittle. On the other hand, the additional curing of ES specimens may have resulted in superior wear resistance compared to AP.

To mechanically fatigue dental restorative materials, laboratory studies can use different laboratory set-ups to apply cyclic loading of a material [21-25]. Cyclic loading

is often performed by an indenter that repeatedly applies either A) a compressive load on the tested material or B) a bending load, needed for flexural testing. The specific configuration used in this study showed that wear and fatigue could be simultaneously employed for restorative materials as the slide motion induces damage by friction between the indenter and the material. In addition, the used configuration could induce subsurface cracks in ceramic and polymer-infiltrated ceramic network materials (PICNs), although no such subsurface cracks were observed for composite materials[16].

5 CONCLUSIONS

This study showed that fatigued ES specimens had poor fatigue resistance and that direct hybrid and direct nanocomposites had equal wear resistance. The indirectly processed composites showed superior wear resistance compared to directly processed composites. These outcomes concur with the outcomes of clinical studies on the longevity of specific composite products in patients with tooth wear [3-5,7,8,16]. The employed laboratory test can be regarded as clinically relevant as clinical presentations were emulated in the laboratory. Moreover, the first step in the translational research cycle has been made with the emulation of clinical presentations in the laboratory; 'from the clinic to the lab'.

6 ACKNOWLEDGEMENTS

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Table 1: Materials in the study including brand names, shades, Inorganic and organic characteristics, and mechanical properties conform the manufacturers

	Manufacturer	Type	Content (w/v)	Organic Composition	Inorganic composition	Particle size	Compressive Strength (MPa) (according to manufacturer)	Young's modulus (GPa) (according to manufacturer)	Flexural Strength (MPa) (according to manufacturer)
Clearfil ™ AP-X	Kuraray Medical, Osaka, Japan	Direct: Micro-hybrid composite	85.5/ 70	- Bis-GMA, - TEGDMA.	Silanated barium glass, Silanated silica, Silanated colloidal silica fillers.	between 0.1 µm and 15 µm (mean; 3 µm).	449	16.8	204
Filtek ™ Supreme XTE	3M ESPE Dental products, Seefeld, Germany	Direct: Nano-composite	72.5/ 55.6	-Bis-GMA, -TEGDMA, -UDMA, -Bis-EMA	Silica filler (20 nm). Zirconia filler (4-11 nm). Cluster of silica and zirconia fillers.	between 0.6 µm and 10 µm (average of cluster).	371	11.3	165
Estenia ™ C&B	Kuraray Medical, Osaka, Japan	Indirect: Micro-hybrid composite	92/82	-BIS-GMA, -UDMA -Hydrophobic aromatic dimethacrylate[2] -Hydrophobic aliphatic methacrylate[2] -Decandiol dimethacrylate[3].	Surface treated alumina (2µm) Silanated glass ceramics dl-Camphorquinone Initiators Accelerators Pigments[2]	0.02 to 2.0 µm	613	28.6	202
Lava Ultimate	3M ESPE Dental products, Seefeld, Germany	Indirect: Nano-composite	80/65	Coupling agent: Silane. -Bis-GMA, -TEGDMA, -UDMA, -Bis-EMA	Silica filler (20 nm), zirconia filler (4-11 nm), Cluster of silica and zirconia fillers.	between 0.6 µm and 10 µm (average of cluster).	383	12.8	204

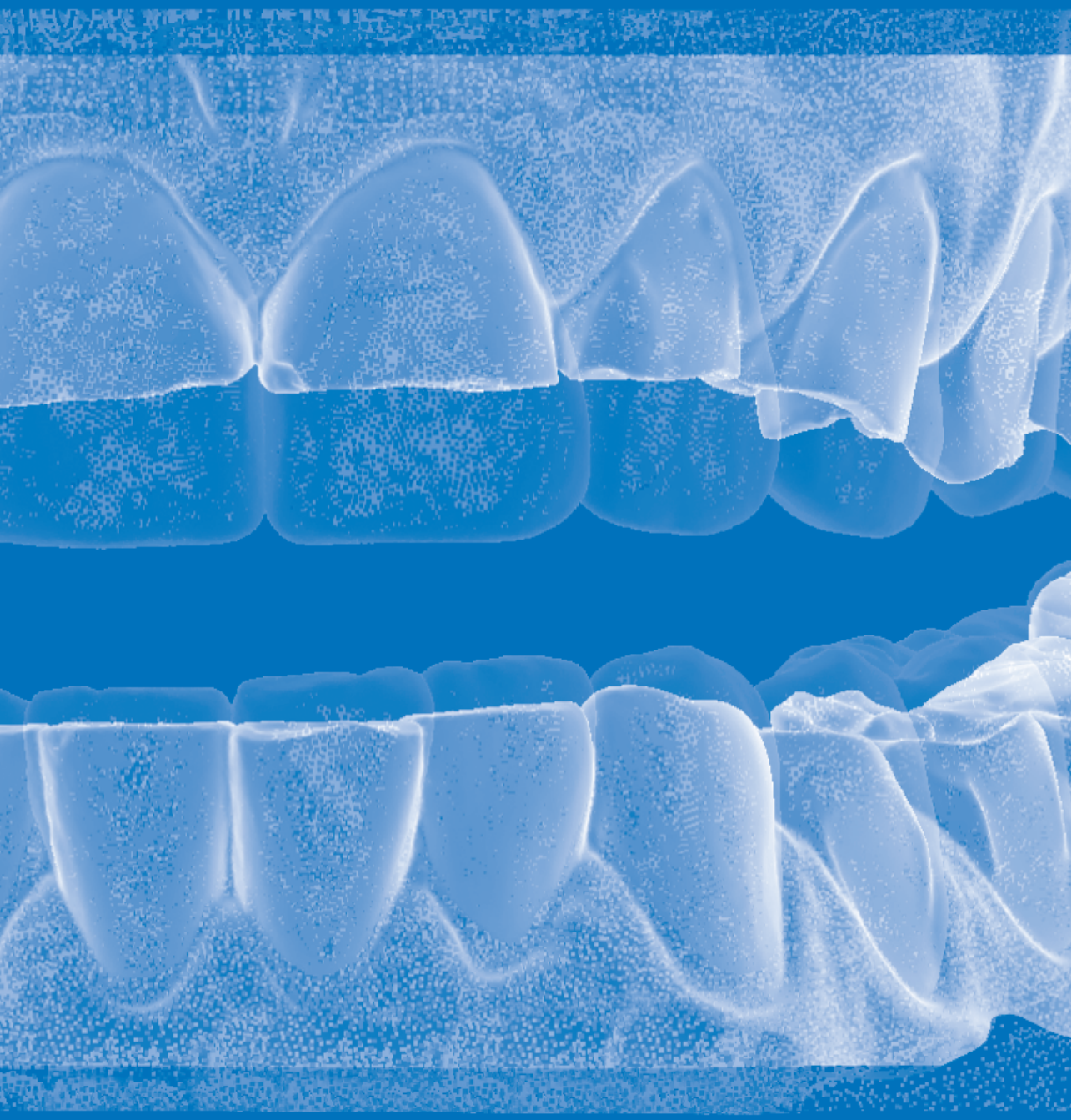
Table 2– Regression analysis of the wear scar

	Estimate (mm^3)	95% CI	P value
Intercept (AP)	0.25	0.194 – 0.302	
ES	-0.08	-0.153 – 0.000	0.05
FS	0.005	-0.074 – 0.085	0.89
LU	-0.09	-0.162 – -0.010	0.03*

Table 3– Regression analysis of the Flexural strength and the effect of the fatigue test.

	Estimate (N)	95% CI	P value
Intercept (AP)	183.5	173.5 – 193.5	
ES	3.3	-10.9 – 17.4	0.65
FS	-65.9	-80.0 – 51.8	<0.001*
LU	-44.6	-58.8 – 30.5	<0.001*
The fatigue test	-9.8	-24.5 – 4.8	0.19
ES + fatigue test	-75.3	-96.1 – 54.6	<0.001*
FS + fatigue test	10.0	-10.7 – 30.8	0.34
LU + fatigue test	18.0	-2.7 – 38.8	0.09

The intercept can be regarded as AP specimens that did not receive the fatigue test. The effect of the material (without fatigue test) on the flexural strength is described for ES, FS, and LU, separately. The Estimate (N) gives the mean change in flexural strength relative to the mean flexural strength of the Intercept group (AP).
'The fatigue test' refers to the effect of the fatigue test on the flexural strength. The ES/FS/LU + fatigue test describes the effect of the fatigue test for each material on the flexural strength.
* = statistical significance was reached



7

GENERAL DISCUSSION

1 AIM OF THE THESIS

The aim of this thesis was to study the minimally invasive restorative treatment approaches for the management of worn dentitions. Considering the complexity, comprehensiveness, and variety of variables that are involved in the longevity of restorative treatment, this thesis can impossibly be complete and all-encompassing. Specific variables in the complex treatment of worn dentitions have been studied and conclusions regarding these variables can be drawn. This thesis gives strong recommendations and insight regarding, 1) the necessity of a tryout of the VDO-increase required for the restorative treatment of tooth wear and the application technique of resin composite restorations i.e., 2) direct application vs 3) conventional indirect application vs 4) CAD/CAM application, 5) fatigue behavior of dental resin composite materials.

2 GENERAL METHODOLOGICAL APPROACH

The Radboud Tooth Wear Project (RTWP) is a clinical project, where patients with tooth wear with diverse levels of dental co-morbidity are managed. Management of tooth wear can range from counselling & monitoring to restorative treatment and its follow-up. In the RTWP, multiple trials are embedded.

This thesis contains, but is not limited to, the reports on a 2x2 factorial design randomized controlled trial (RCT) and a prospective trial embedded in the RTWP [1]. For pragmatic research purposes, only patients with tooth wear with limited levels of dental co-morbidities, such as multiple missing teeth, periodontal disease, and/ or signs of dental caries, were included in the trials. Figure 1 is an example of a typical patient in the trials embedded in the RTWP. These co-morbidities are likely to influence the longevity of the restorative intervention, compromising the research objectives. Restorative treatment of worn dentitions with dental co-morbidities involves even more complex treatment with more (confounding) variables included, making adequate comparisons between groups more complex. In addition, the inclusion of patients with higher levels of dental comorbidities could have contributed to an inclusion bias. In The Netherlands, patients with severe generalized tooth wear are reimbursed for the expenditure of restorative treatment from their universal insurance only when no significant dental comorbidity is present. In patients with higher levels of comorbidity, the restorative treatment of tooth wear is not reimbursed. So, patients would need to pay for the proposed treatment. Taking the extent of treatment into consideration, it would involve significant costs for patients. Some patients, meeting all eligibility criteria, but

unable to pay for the treatment, would not be included, and this would contribute to inclusion bias. All things considered; the outcomes of the presented studies cannot be generalized to all patients with tooth wear.

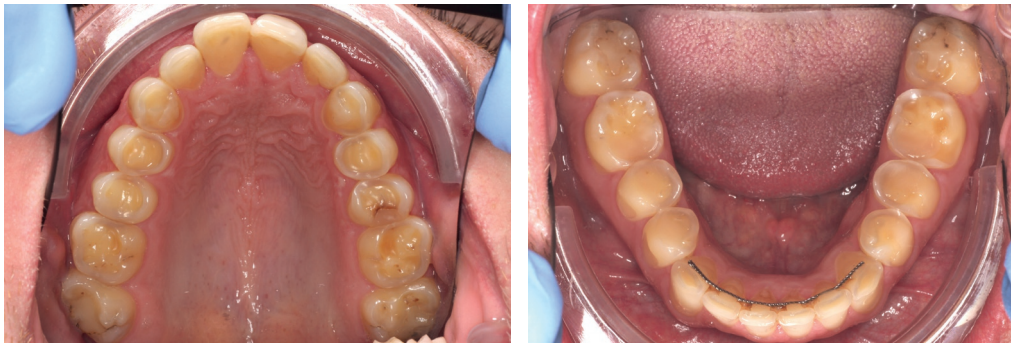


Figure 1: Typical patient in the trials of the RTWP. This patients has generalized tooth wear without dental comorbidities; no missing teeth and few restorations.

Prospective trials in restorative dentistry often exclude 'high risk' patients from their study population e.g., high caries risk patients and patients with tooth wear[2,3]. Rather than including patients that need restorative treatment because of active dental disease, they preferably include healthy patients that require restorative treatment as a consequence of 'maintenance care'. This is understandable, as these studies strive to show good performance of restorative work. However, restorative work in these healthy, 'low-risk' patients generally show good clinical outcomes[4-6]. To yield statistically significant differences, clinical studies require larger sample sizes and longer observation periods given the adequate clinical performance of the 'gold standard' technique. This increases the investment in already resource-intensive studies. Also, studies comparing a new, supposedly improved, material/technique vs. the current material/technique might not have high clinical relevance if the existing standard already performs sufficiently. [7]

"Trials in restorative dentistry should focus on high-risk patient groups and should include patients with signs of active disease"

It is increasingly recognized that other factors than materials and techniques influence the longevity of restorations, e.g., caries risk, habits of tooth grinding and clenching, socio-economic status, and operator variables. [8-13]. Restorative work in patients with high caries risk is mainly limited by (secondary) caries and in patients with tooth wear, it is mainly limited by fracture and wear.[13] Trials in restorative dentistry should therefore focus on high-risk groups and include patients with

signs of active disease. The studies presented in this thesis specifically included those patients that are excluded in regular trials in restorative dentistry. Eligibility criteria for the trials embedded in the RTWP were chosen to specifically include high-risk patients with active disease, i.e., tooth wear. However, including patients with (almost) complete dental arches resulted in the exclusion of patients that may have suffered vertical fractures of (sound) teeth as a result of extravagant clenching forces. Such 'extremely high-risk' patients were not included in the trials within the RTWP. This may limit the external validity of the presented outcomes.

3 TRANSLATIONAL RESEARCH

The classical direction of evaluating the performance of dental materials is to initially perform laboratory studies to predict *in vivo* results prior to undertaking clinical trials. Clinical trials are the gold standard in evaluating the performance of dental materials. There is always the initial need for *in vitro* studies to analyze and examine basic biological and mechanical effects and phenomena, and to compare them to gold standards, as *in vitro* studies require less time and less finances than clinical trials. Unfortunately, *in vitro* tests struggle with their clinical relevance. *In vitro* outcomes on restorative materials or adhesive dentistry so far do not predict *in vivo* outcomes very well. Translational research focuses on identifying clinically relevant aspects from the clinic, first, and then tries to reproduce a specific clinical phenomenon in laboratory set-ups [14]. When it is successfully reproduced, a laboratory set-up can be regarded as 'clinically relevant'. Subsequently, modifications to the clinically relevant aspects can be introduced in the laboratory to predict and optimize *in vivo* outcomes. This can be regarded as a translational research cycle characterized by *'from clinic to lab and then back to clinic'*.

The *in vitro* study in this thesis displays data that is supplementary to the clinical data. It can be regarded as the first step (*clinic to lab*) in the translational research cycle. The composite materials that were used in the clinical trials embedded in the RTWP were additionally tested in the laboratory study. In these clinical trials, it was observed that the conventional posterior indirect composite restorations demonstrated a significantly inferior performance (chapter 2) compared to the directly applied micro-hybrid composite restorations. It was also observed that the amount of contact wear for nanocomposites and micro-hybrid composites was similar, *in vivo* [15]. To better understand the materials' effect on longevity and behavior in the clinical setting, we evaluated specific mechanical properties of the materials i.e., fracture strength, mechanical fatigue resistance, and wear resistance. In the laboratory setup, both the inferior performance of Estenia C&B and similar levels of contact wear for micro-hybrid composites and nanocomposites were observed.

4 CASE SELECTION

Patients included in the different trials embedded in the RTWP have a mean age of 38 years. This may be considered to represent a reasonably young sample of patients. As described above, the eligibility criteria contributed to the inclusion of relatively younger patients. When restoratively treating young patients, operators should bear in mind the restorative repeat cycle in dentistry[16]. It is likely that a second or even a third restorative intervention will be required in the future for these patients. Therefore, subtractive approaches are not recommended and the longevity of conventional circumferential ceramic crowns in these patients was not one of the research aims[17]. Minimally invasive, additive restorative approaches using direct composite restorations or indirect 'tabletop' restorations, however, were.

One of the difficulties interpreting the presented results in this thesis for general practitioners is that the operators in the trials of the RTWP were all trained in adhesive dentistry and the undertaking of full mouth rehabilitations with directly applied composite restorations. For general dental practitioners that are less trained in these procedures, outcomes may be different. It is highly recommended that practitioners consider seeking comprehensive training and continuing education to ensure that they are fully equipped with the necessary skills and expertise before undertaking intricate dental treatments, in order to provide the best possible care for their patients.

Treatments in (general) health care should logically be beneficial for the patient's health and their overall quality of life. The restorative treatment of tooth wear in the RTWP resulted in a substantially improved Oral Health-Related Quality of Life (OHRQoL)[18]. Case selection may be a reason in this observation, as an important inclusion criterium for restorative treatment was the presence of a demand for restorative treatment by the patient. Patients with moderate to severe tooth wear, without such a demand, were always treated by 'counselling and monitoring'. So, the patients that received restorative treatment all had moderate to severe tooth wear and clearly impaired oral functioning, e.g., hypersensitivity and unsatisfactory aesthetics. These patients, especially, benefit from restorative treatment, resulting in an improved OHRQoL, which is increasingly recognized as an important outcome measure of treatment in health care studies. Moreover, this may have contributed to the high recall percentages (>95% after 5 years) in the trials of the RTWP.

5 OUTCOME MEASURES

Failure of restorations is one of the main outcomes of this thesis. As failure criteria may vary, with important effects on conclusions, we assessed multiple criteria for failure. The criteria were all clinically driven, as they reflected the choice of the clinician (either the general dental practitioner or a clinician in the RTWP) on interventions to restorations. Interventions could be replacement, repair, or refurbishment by polishing in case of a small material fracture (Fig 2). Scoring of restorations was done clinically in combination with 3D scans. The decision on the type of intervention needed may have been operator-dependent, as different operators may have had different attitudes towards performing a restorative intervention when for example, 'only' a small material fracture was present and the patient did not have any symptoms or even was unaware of the fracture. The decision to intervene (or not) was always made in conjunction with the patient, as part of a shared decision-making process.

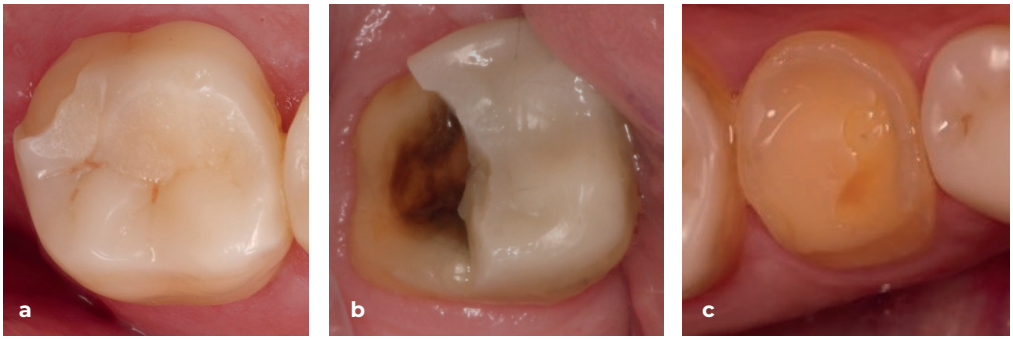


Figure 2: a: Restoration that needed refurbishment by polishing, b: restoration that needed repair, c: restoration that needed replacement

Endpoints in longevity for restorations are easily detected when (large) fractures of restorative material take place, as they are readily detected on visual inspection. They were also 'double-checked' on (greyscale) intra-oral 3D scans. Endpoints in the longevity of restorations due to contact wear are less clear. For restorations in regular patients, wear or restorations is not a clinical problem that requires additional care[13]. For these high-risk patients, however, contact wear is a significant problem that may necessitate a subsequent round of restorative treatment to maintain optimal oral health and functionality for the patient. Most prospective trials in restorative dentistry apply FDI criteria [19] or USPHS[20] criteria [21] to objectify differences over time. Wear of restorations is then assessed as 'excessive wear', 'alteration of occlusal contour', or 'lost occlusal contact points'. For the build-up

restorations in these treatments, such criteria are not applicable. Even at more advanced stages of wear, restorations in our studies did not receive restorative care, as the decision to repair or replace a worn restoration is generally not made at a tooth level but at arch level, or even at patient level. This would require a new round of restorative care, which none of the patients in these studies, with limited observation time, have received.

6 GENERAL RESULTS AND CONSEQUENCES FOR GENERAL PRACTITIONERS AND RESEARCH

Restorative treatment of tooth wear in this thesis focused on a minimally invasively, additive approach. These restorations function as a 'protective layer' at the worn teeth, which simultaneously improves the OHRQoL and orofacial aesthetics. When the clinical success of the restorations was limited, it was mainly limited by the incidence of fracture (and not debonding or caries). Studies on the performance of composite restorations in patients with tooth wear often evaluate directly applied composite restorations[20]. Most studies, including the outcomes of the present RCT, indicate acceptable clinical performance of this technique in these patients in the short and mid-term[20]. Within the observation time of the studies, the impact of wear of the restorations on their clinical performance was limited. However, based on outcomes of wear measurements of these restorations it is expected that it may hamper the clinical performance of these restorations, in the long term[15,22].

Indirect composite restorations can be processed under ideal circumstances, promoting the mechanical characteristics of the material, including wear resistance. Indirect techniques may therefore, in the long term, provide superior protection to worn-down teeth. Another advantage of indirect composites may be the need for a less complex clinical procedure, as both the shaping of restorations and the planning of VDO-increase are performed extra-orally. That may contribute to the attainment of a more predictable procedure. It is, thus, important to explore indirect techniques for the minimally invasive restorative treatment of tooth wear and to study materials and manufacturing processes, especially with the increasing presence of 3D scanners in general practices (in the Netherlands).

Three restorative managements were studied in this thesis; directly applied composite, conventional indirectly applied composite, and CAD/CAM composite. These outcomes cannot be directly compared, as they were part of separate trials. However, both trials had similar inclusion and exclusion criteria, making careful comparison possible. Conventional posterior indirect composite showed poor

clinical performance, whereas directly applied composite and CAD/CAM composite both showed more than acceptable clinical performance [23,24]. For load-bearing areas at the anterior regions, where the applied load during functioning was lower, all treatment modalities showed good performance in the short- or mid-term. A likely important condition relating to the clinical performance of resin composite restorations is the volume and thickness of restorative material that was applied. The objective was not to restore teeth to their anatomically correct dimensions, but, where possible, restorations were made thick and 'bulky,' to give restorations maximum mass and volume on the assumption this would contribute to their strength. Clinical data on the longevity of resin composite restorations that were placed in the restorative treatment of tooth wear in which a higher VDO-increase was realized had a lower risk for restoration failure[25].
It is difficult to identify a specific factor that was responsible for the poor clinical performance of conventional indirect restorations on molars, while CAD/CAM indirect restorations had an acceptable clinical performance. Amongst the possible factors is the layer thickness of the restorations. The mean VDO-increases at first molars in patients that were treated with conventional indirect composite restorations and in patients that were treated with CAD/CAM composite restorations were 2.2(±0.7) and 2.8(±0.7) mm, respectively. From the applied increase in VDO, it can be seen that the CAD/CAM composite restorations were thicker than the conventional indirect restorations.

A second possible reason for the better clinical outcomes of the indirect CAD/CAM restorations may be the manufacturing process. These restorations are digitally designed and milled from pre-polymerized blocks which were produced under 'industrial' circumstances. The material is optimally processed and likely functions as a 'monobloc'. Conventional indirect restorations, on the other hand, are handcrafted and are built up in multiple layers into an anatomically correct form by a dental technician. This may reduce the ability of the restoration to function as a 'monobloc', because 'imperfections', such as voids. Critical stress limits that result in fracture of the material, are more quickly reached when an imperfection is present.

A third possible factor may be the fatigue resistance of specific materials. The conventional indirect composite also showed poor fatigue resistance in the *in vitro* set-up, while other materials showed good fatigue resistance, similar to clinical findings.

A fourth factor influencing the clinical performance of the conventional indirect composite may have been the fit of restorations. Whilst the fit of the CAD/CAM restorations was considered to be 'precise' by the operators, conventional indirect

restorations were deemed to offer a looser fit, possibly compromising the seating of restorations and an inequal cement layer thickness of the underlying cement.

Which subtype of composite should be used when restoring a worn dentition? There is no strong evidence to suggest that any material is better than another,[26] as there is a lack of randomized controlled trials comparing different subtypes of composite e.g., hybrid vs nanocomposite, in patients with tooth wear. There is one subtype of composite that is ill-advised. Micro-filled composites have been suggested to show poor clinical performance, as material fracture was frequently observed [27]. Micro-filled composites were not used in the RTWP. Within the RTWP both micro-hybrid composites and nanocomposites were used. No data on the performance of nanocomposites are yet available. However, when comparing micro-hybrid composites to nanocomposite restorations, similar levels of contact wear were observed *in vivo* [15], suggesting that both materials can be used in patients with tooth wear. These findings are also congruent with the outcomes of the present *in vitro* study, which showed similar levels of contact wear for the two direct composites (nano vs micro-hybrid) and the two indirect composites (nano vs micro-hybrid).

When restoring generalized tooth wear, is it necessary to test the VDO-increase before the commencement of restorative treatment? Some studies advocate the necessity of a "test drive" of the VDO-increase [28-30]. This additional step in the restorative approach may help to identify patients that have difficulties with adapting to the VDO-increase, which might require adaptation of the restorative treatment plan. None of the patients in the trials of the RTWP had reported maladaptation to the VDO-increase either with or without a test drive of the VDO-increase. That indicates that the VDO-increase needed for these rehabilitations is accepted by patients. The RCT was performed to evaluate the test drive on its merits for the patient (OHRQoL + early restoration failure) and the dentist (early restoration failure). Patients reported that the wearing of the removable appliance was uncomfortable and (thus) reported poor compliance. The outcomes of this study suggest no beneficial effect of evaluating the VDO-increase. Omitting the tryout from these restorative treatments results in reduced strain for patients and treatments that are less time-consuming and less expensive. In younger patients with generalized tooth wear, the VDO can be safely increased up to approximately 5 mm. Regarding the homogeneity of the studied patients, these recommendations have limited external validity. For older patients, or patients with (a history of) temporomandibular dysfunction that need a VDO-increase, a test drive may still be needed. It may also still be needed when an extensive restorative rehabilitation using conventional indirect ceramic restorations, that do not allow for major adjustments after placement, is planned. When introducing a VDO-increase of more than 5 mm in any patients, it is still advisory to test the VDO-increase[31].

In the RTWP, no trials with ceramic restorations have been included. Studies on the clinical performance of 'moderately invasive' lithium disilicate restorations[32,33] or invasive traditional ceramic (lithium disilicate and zirconium) crowns[34] for the restorative treatment of tooth wear suggest low fracture and contact wear levels in the mid-term. Prospective trials on the performance of minimally invasive lithium disilicate (or other ceramic) restorations in these patients are lacking in the RTWP. However, the costs of a prospective trial with ceramic restorations, especially, are high. This would possibly lead to an inclusion bias as patients without financial possibilities would have to be excluded, although 'clinical' eligibility criteria are met, as was the case in the latter named study[34].

7 PREDICTIVE FACTORS FOR RESTORATION FAILURE

The results of the present *in vitro* study suggest that mechanical fatigue tests should be incorporated for evaluating restorative materials in a laboratory set-up. Also, contact wear evaluation should be performed whenever their indication for usage in restorative treatment of tooth wear is studied. However, clinical trials remain the gold standard for the evaluation of new restorative treatments.

The clinical presentation of worn dentitions may also predict the risk of restoration failure. Patients with a dominant mechanical etiology are likely to have different patterns of tooth wear and to show higher failure rates (due to fracture) compared to patients with a dominant chemical etiology. From this thesis, it was found that discriminating between these phenotypes of tooth wear is difficult, as there is a high degree of overlap of clinical presentation of these phenotypes. Also, patients often present themselves at different stages of tooth wear, making case selection difficult. That is also one of the reasons why specific etiologies of tooth wear were not regarded as exclusion criteria in the RTWP, or why no stratification for specific etiology was used in the RCT. However, the patient factor is unmistakably involved in the clinical performance of restorations. In the presented studies, a small group of patients was responsible for the majority of restoration failures that were observed. Overall, approximately 10% of the patients were responsible for >50% of the restoration failures. This may be related to the etiology of tooth wear. In the prospective study on CAD/CAM restorations, it was observed that patients that had multiple characteristics of tooth wear with a dominant chemical etiology, had a lower risk for restoration failure than patients with tooth wear without these characteristics. This study also indicates that to discriminate between tooth wear patients with high mechanical risk and low(er) mechanical risk, clinicians should not focus on the presence of mechanical tooth wear features but rather focus

on the absence of chemical tooth wear features. A successful discrimination of the etiology of tooth wear can be a valuable aid in the clinical management of tooth wear. It can improve personalized preventive measures and a personalized estimation of risks involved in the (restorative) treatment (in the long term).

8 FUTURE PERSPECTIVES

Restorative dentistry plays a role in the clinical management of tooth wear, a common dental condition that can significantly impact patient's oral health and quality of life. Within this thesis, various therapies have been studied in this thesis to determine their clinical success in the restorative treatment of tooth wear, including directly applied composite, conventional indirectly applied composite, and CAD/CAM composite restorations.

While the current studies have provided valuable insights into the clinical success of different restorative therapies for tooth wear, it's important to note that outcomes may evolve with longer observation times. The initial success of restorative treatments may be influenced by various factors, such as changing lifestyles, fatigue and or wear of the restorative material, and aesthetic appearance of restorations, which can change over time and affect the longevity of restorations. Long-term observations are essential for evaluating the durability of these restorative treatments. Therefore, follow-up studies with extended observation periods are warranted to better understand the outcomes of different restorative approaches in restoratively treating tooth wear in the long run.

Depending on the condition of the existing restorations, a consecutive round of restorative therapy may be indicated, to maintain oral health and optimal functionality for patients. The approach for the consecutive round can involve either the removal of old restorative material followed by application of the new restorative material or by simply adding new restorative material, without the removal of the old restorative material. In the first approach, restorations are replaced, while in the latter approach restorations are repaired. The latter approach would require less time and may therefore benefit patients and operators. On the other hand, outcomes of new material adhered to old material may adversely affect the longevity of these restorations. This could be a future direction for both clinical and laboratory studies. The laboratory set-up that was used in the presented *in vitro* study, seems well-suited for such a clinical question as clinical outcomes could be emulated *in vitro*, making the laboratory set-up clinically relevant. Different treatment strategies can be tested *in vitro* to better anticipate their clinical behavior.

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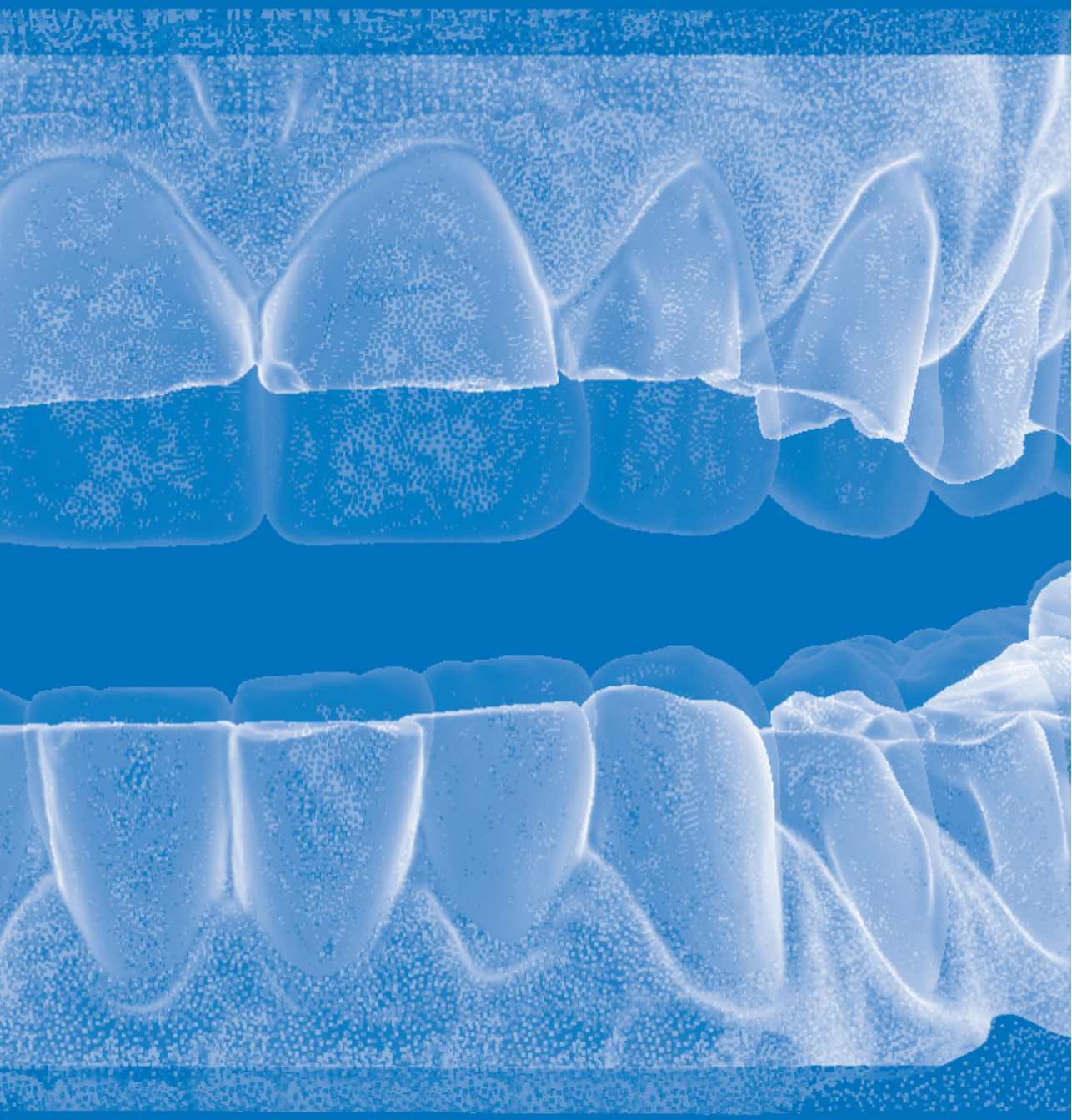


8

SUMMARY | SAMENVATTING

SUMMARY

The primary objectives of this thesis were to evaluate the clinical outcomes of three minimally invasive restorative treatment approaches with composite restorations for patients with generalized tooth wear. Secondary objectives were to evaluate the need to functionally test the planned Vertical Dimension of Occlusion prior to delivery of restorations and to evaluate the in vitro fatigue behavior of composite materials that were employed in the Radboud Tooth Wear Project (RTWP), with a translational approach.

The nature of tooth wear, its etiology, and clinical management, including the principles of restorative treatment and longevity of the restorative treatment, are described in **Chapter 1**. This chapter also describes the RTWP which is the source of the clinical data that is used in this thesis.

A consequence of the minimally invasive restorative treatment of tooth wear is the introduction of an increase in the Vertical Dimension of Occlusion (VDO). The VDO increase may be 3 mm or more to create sufficient interocclusal space for the restorations. When the need for the VDO increase is equivalent to or greater than the clinical resting position of the mandibula, functional problems may be introduced. **Chapter 2** focuses on the need to functionally test the planned VDO increase prior to the application of restorations using an acrylic removable appliance (RA). In an RCT, 42 patients with moderate to severe tooth wear without (a history of) temporo mandiblar dysfunction, were randomly allocated to either a test phase with a RA for 3 weeks or no test phase. Restorative treatment consisted of the restoration of all teeth using composite restorations with a VDO increase. The Oral Health-Related Quality of Life (OHRQoL), freeway space (FWS), and clinical acceptability of restorations were assessed at baseline and recall appointments (1 month and 1 year). Interventions to restorations were scored in case of material chipping or when the abutment tooth had increased sensitivity that could be linked to occlusal overloading. Clinical follow-up was completed for 41 patients. The mean realized VDO-increase measured at first molars was 2.3 mm (± 0.6). No significant effect of the test phase on the OHRQoL after 1 month ($p=0.14$), nor after 1 year ($p=0.76$) could be found. No significant effect of the test phase on the FWS after 1 month could be found in the ANCOVA analysis ($p=0.69$). However, ANCOVA analysis showed that the FWS in the RA group was significantly lower after 1 year ($p=0.01$). No effect could be observed on the number of interventions that were needed for the restorations within the observation time. Evaluated from the perspective of the patient and the operator, no beneficial effects of the test phase using a RA for three weeks on the treatment as a whole were observed.

Chapter 3 describes an RCT, aimed to evaluate the survival and failure behavior of Direct Composite Restorations (DCR) and conventional Indirect Composite Restorations (ICR) on molars and anterior teeth. Forty-two patients with generalized moderate to severe tooth wear with a need for restorative treatment were included and were randomly assigned to one of 2 protocols: (1) DCR: All teeth were restored with directly applied micro-hybrid composite restorations (Clearfil AP-X, Kuraray) for load bearing areas and nano-hybrid composite restorations (IPS Empress Direct, Ivoclar Vivadent) for buccal veneers; (2) ICR: First molars were restored with indirect composite 'tabletop' restorations and maxillary anterior teeth were restored with indirect palatal veneer restorations (Clearfil Estenia C&B, cemented with Panavia F, Kuraray). The remaining teeth were restored directly. Restorations were evaluated after 1 month, 1 year, and 3 years, focusing on clinical acceptability. Three levels of failure were recorded: Level 1 failure = a restoration that required replacement (or in case of tooth extraction); Level 2 failure = a restoration that required a repair; Level 3 failure = a restoration with small material chips (that received either refurbishment by polishing or needed no further treatment). Statistical analysis was performed using Kaplan-Meier curves, Annual Failure Rates (AFRs), and univariate Cox regression analyses. Four hundred eight restorations on first molars and palatal veneers on maxillary anterior teeth were part of this RCT, with 220 DCR and 188 ICR. No differences in survival between DCR and ICR for palatal veneer restorations for any failure criteria were found. Tabletop restorations on first molars showed a considerably higher failure rate for ICR compared to DCR ($p=0.026$, HR: 3.37, 95%CI= 1.16-9.81).

These findings illustrate that the used conventional ICR had poor clinical success and that DCR, with maintenance, can provide an acceptable mid-term option for the treatment of severe, generalized tooth wear. Novel techniques may improve the clinical success of ICR and **Chapter 4** describes a case report of a digital workflow that was applied to restore a severely worn dentition with minimally invasive indirect CAD/CAM resin nano-ceramic restorations. The patient with generalized severe tooth wear had a clear demand for treatment as he suffered from dentin hypersensitivity and wanted to improve the aesthetic appeal of his dentition. The etiology of tooth wear was multifactorial; habits of tooth grinding, frequent acidic intake, and Gastroesophageal reflux disease (GERD). The new VDO was determined and the desired new VDO was registered using silicone stops in the posterior area. After teeth were prepared for the indirect restorations. Preparation was limited to (1) taking away sharp ridges and (2) a small chamfer to provide the outline of posterior occlusal surfaces. Digital impressions were made, and the digital bite registration was completed with the silicone stops in situ. A fully digital wax-up was made by a dental technician. Tabletop restorations on (pre)molars were digitally

designed and labial and palatal veneer restorations were designed for mandibular anterior teeth and maxillary anterior teeth, respectively. The cementation of the CAD/CAM restorations was completed in two separate sessions. After cementation of all indirect restorations, direct veneer restorations on maxillary anterior teeth were made to improve the aesthetic appeal.

A fully digital workflow showed a good functional and aesthetic outcome of the restorative treatment. However, no information on the clinical success in the short-term of these restorations was available. This prospective study is described in **Chapter 5**. The aim was to evaluate the clinical performance of minimally invasive CAD/CAM nano-ceramic restorations in the restorative treatment of generalized tooth wear. The CAD/CAM restorations were placed on all teeth and were evaluated on their clinical acceptability after 1 month and after 1 year. Similar failure levels for the restorations as described in chapter 3 were used. Additionally, the OHRQoL was assessed at baseline and after 1 year. Twenty-one patients (age: 41.7 ± 10.4y) were evaluated after 1 year (13.5 ± 1.2m). Five hundred eight indirect CAD/CAM restorations were placed. None were replaced or lost. Twelve were repaired and ten were refurbished. Success percentages were 100% to 97.2%. The restorative treatment had a significant positive impact on the OHRQoL ($p<0.001$). Additionally, two features of mechanical tooth wear and three features of chemical tooth wear were scored at baseline. The association of restoration failure with tooth wear etiology was analyzed using a multilevel logistic regression analysis, with a random intercept for patients. The presence of 1 or 2 features of mechanical tooth wear showed no significantly increased risk of restoration failure ($p=0.78$). The presence of 2 or 3 features of chemical tooth wear, compared to the absence of these features resulted in a significantly lower risk of restoration failure ($p=0.002$).

These findings show that minimally invasive CAD/CAM nano ceramic restorations perform satisfactorily in the short term. Other prospective studies embedded in the RTWP and the study described in chapter 3 showed acceptable clinical performance of directly applied composite restorations. It is unclear why the conventional ICR, as described in chapter 3, performed inferiorly compared to the CAD/CAM restorations and the DCR. **Chapter 6** describes a study that aimed to reproduce and translate clinical presentations in an in vitro setup and aimed to evaluate laboratory outcomes of mechanical properties and link them to the clinical outcomes of the employed materials in the studies of the RTWP. Thirty disc-shaped specimens (Ø12.0 mm, 1.2 mm thick) of four composites were fabricated (Clearfil TM AP-X (AP), Filtek TM Supreme XTE (FS), Estenia TM C&B (ES), and Lava Ultimate (LU)). Cyclic loading (200N, 2Hz frequency, was applied concentrically to 15 specimens per composite with a spherical steatite indenter (r=3.18mm) in water in a contact-

load-slide-and-back motion (10^5 cycles). Cyclic loading resulted in a wear scar on the specimens' surface. The wear scar was analyzed using profilometry and virtual computation of the volume. All specimens were loaded until fracture in a biaxial flexural strength setup. The effect of the material on the volume of the wear scar was evaluated with a regression analysis. With AP as a reference group, FS showed a similar degree of volume loss, but both the indirect composites had significantly lower volume loss. The flexural strength of the composite discs was analyzed for the effect of the material, the effect of the fatigue test, and the interaction between the material and the fatigue test. With non-fatigued AP as a reference group, non-fatigued ES specimens had similar flexural strength. FS and LU had significantly lower flexural strength compared to AP. For ES specimens only, an interaction between the fatigue test and the material could be observed ($p<0.001$; 95%CI: -96.1 - -54.6). This study showed that fatigued ES specimens had poor fatigue resistance and that direct hybrid and direct nanocomposites had equal wear resistance. The indirectly processed composites showed superior wear resistance compared to directly processed composites. These outcomes concur with the outcomes of clinical studies in the RTWP. The employed laboratory test can be regarded as clinically relevant as clinical presentations were emulated in the laboratory. Moreover, the first step in the translational research cycle has been made with the emulation of clinical presentations in the laboratory; 'from the clinic to the lab'.

Chapter 7 discusses the results of the included studies, and it discusses directions for further research.

In conclusion, the main purpose of this thesis was to study the minimally invasive restorative treatment approaches for the management of moderate to severe tooth wear. Specific variables in the complex treatment of worn dentitions have been studied. We can conclude that a try-out of the new VDO prior to restorative treatment using a RA has no beneficial effect on the restorative treatment. Directly applied composite restorations show acceptable results in the mid-term when used in these complex rehabilitations, although maintenance by polishing and occasional repairs are needed. Conventional indirect composite restorations are not suitable in the posterior area, while CAD/CAM restorations seem to be a viable alternative to indirectly restore a worn dentition. Additionally, we can conclude that it was possible to emulate specific clinical outcomes of the RTWP in a laboratory setup. The conventional indirect composite showed poor fatigue resistance in the laboratory setup. Poor fatigue resistance could be a decisive factor in the poor clinical outcome of the conventional indirect restorations.

SAMENVATTING

De primaire doelstelling van dit proefschrift was het evalueren van de klinische resultaten van drie minimaal invasieve restauratieve behandelingen met composiet restauraties voor gegeneraliseerde gebitsslijtage. Secundaire doelstellingen waren het evalueren van de noodzaak om de geplande verticale dimensie van occlusie functioneel te testen voorafgaand aan het aanbrengen van restauraties én het *in vitro* evalueren van de vermoeiing van composietmaterialen die werden gebruikt in het Radboud Tooth Wear Project (RTWP), met een translationele aanpak.

De aard van gebitsslijtage, de etiologie en het klinisch beleid van de zorgverlener, evenals de principes van restauratieve behandeling en haar levensduur worden beschreven in **hoofdstuk 1**. Ook wordt hier het RTWP beschreven. Dit is de bron van de klinische data die in dit proefschrift worden gebruikt.

Een gevolg van de minimaal invasieve restauratieve behandeling van gebitsslijtage is het introduceren van een beetverhoging, ofwel een toename van de Verticale Dimensie van Occlusie (VDO). De VDO-verhoging kan 3 mm of meer bedragen om voldoende interocclusale ruimte te creëren voor de restauraties. Wanneer de noodzaak van de VDO-verhoging gelijk is aan of groter is dan de klinische rustpositie van de mandibula, kunnen er functionele problemen ontstaan. **Hoofdstuk 2** richt zich op de noodzaak om de geplande VDO-verhoging functioneel te testen voorafgaand aan het aanbrengen van restauraties met behulp van een uitneembare voorziening (UV). In een RCT werden 42 patiënten met matige tot ernstige gebitsslijtage zonder (een voorgeschiedenis van) temporo mandibulaire disfunctie, willekeurig toegewezen aan ofwel een testfase met een UV gedurende 3 weken ofwel geen testfase waarna gebitsslijtage restauratief werd behandeld. De restauratieve behandeling bestond uit restauratie van alle tanden en kiezen met composiet restauraties met een VDO-verhoging. De Oral Health-Related Quality of Life (OHRQoL), freeway space (FWS), en klinische status van de restauraties werden beoordeeld bij baseline en recall afspraken (1 maand en 1 jaar). Interventies aan restauraties werden gescoord in geval van materiaal chipping of wanneer het element een verhoogde gevoeligheid had die in verband kon worden gebracht met occlusale overbelasting. Klinische follow-up werd voltooid voor 41 patiënten. De gemiddelde gerealiseerde VDO-verhoging gemeten bij de eerste molaren was 2,3 mm (± 0,6). Er werd geen significant effect gevonden van de testfase op de OHRQoL na 1 maand ($p=0,14$), noch na 1 jaar ($p=0,76$). In de ANCOVA-analyse werd geen significant effect van de testfase op de FWS na 1 maand gevonden ($p=0,69$). Uit de ANCOVA-analyse bleek echter dat de FWS in de UV-groep na 1 jaar significant lager was ($p=0,01$). Er kon geen effect worden waargenomen op het aantal interventies

dat nodig was voor de restauraties binnen de observatietijd. Beoordeeld vanuit het perspectief van de patiënt en de behandelaar werden geen positieve effecten van de drie weken durende testfase met een UV op de behandeling als geheel waargenomen.

Hoofdstuk 3 beschrijft een RCT die de overleving en het faalgedrag van Directe Composiet Restauraties (DCR) en conventionele Indirecte Composiet Restauraties (ICR) op molaren en frontelementen evalueert. 42 Patiënten met gegeneraliseerde matige tot ernstige gebitsslijtage met behoefte aan restauratieve behandeling werden geïncludeerd en zijn willekeurig toegewezen aan een van de twee protocollen: (1) DCR: alle tanden werden gerestaureerd met direct aangebrachte micro-hybride composietrestauraties (Clearfil AP-X, Kuraray) voor belastbare regio's en nano-hybride composietrestauraties (IPS Empress Direct, Ivoclar Vivadent) voor buccale veneers; (2) ICR: Eerste molaren werden gerestaureerd met indirecte composiet 'tabletop' restauraties en voortanden in de bovenkaak werden gerestaureerd met indirecte palatinale veneer restauraties (Clearfil Estenia C&B, gecementeerd met Panavia F, Kuraray). De overige elementen werden gerestaureerd met directe composiet restauraties. De restauraties werden na 1 maand, 1 jaar en 3 jaar geëvalueerd op klinische aanvaardbaarheid. Er werden drie faalniveaus geregistreerd: Niveau 1 falen = een restauratie die vervangen moest worden (of in geval van extractie); Niveau 2 falen = een restauratie die gerepareerd moest worden; Niveau 3 falen = een restauratie met kleine materiaal chipping (die gereviseerd werd door polijsten of die geen verdere behandeling nodig had). Statistische analyse werd uitgevoerd met behulp van Kaplan-Meier curves, jaarlijkse faalpercentages (AFR's) en univariate Cox-regressieanalyses. 408 Restauraties op eerste molaren en palatinale veneers op maxillaire frontelementen maakten deel uit van deze RCT, met 220 DCR en 188 ICR. Er werden geen verschillen in overleving gevonden tussen DCR en ICR voor palatinale veneer restauraties voor alle faalcriteria. Tabletop restauraties op eerste molaren vertoonden een aanzienlijk hoger jaarlijks faalpercentage voor ICR in vergelijking met DCR (p=0,026, HR: 3,37, 95%CI= 1,16-9,81).

Deze bevindingen illustreren dat de gebruikte conventionele ICR een matig klinisch succes had en dat DCR een aanvaardbare optie op middellange termijn kan zijn voor de behandeling van ernstige, gegeneraliseerde gebitsslijtage. Nieuwe technieken kunnen het klinische succes van ICR verbeteren en **hoofdstuk 4** beschrijft een case report van een digitale workflow die werd toegepast om een dentitie met gegeneraliseerde ernstige gebitsslijtage te herstellen met minimaal invasieve indirecte, CAD/CAM-vervaardigde nanokeramische restauraties. De patiënt had een duidelijke zorgvraag voor behandeling, omdat hij last had van overgevoeligheid

van het dentine en een esthetische verbetering van zijn gebit wenste. De etiologie van de gebitsslijtage was multifactorieel; gewoontes van klemmen en knarsen, frequente inname van zuur dieet en gastro-oesofageale refluxziekte (GERD). De nieuwe VDO werd bepaald en geregistreerd met behulp van siliconen 'stops' in de posterieure regio. Waarna de elementen werden geprepareerd voor de indirecte restauraties. Dit werd beperkt tot (1) het wegnemen van scherpe randen en (2) een kleine chamfer om de contouren van de toekomstige restauratie aan te geven. Er werd een 3D-scan gemaakt en de digitale beetregistratie werd voltooid met de 'stops' *in situ*. Een volledig digitale wax-up werd gemaakt door een tandtechnicus. Tabletop restauraties op (pre)molaren en buccale en palatale veneer restauraties werden digitaal ontworpen voor elementen in respectievelijk het onderfront en het bovenfront. Het cementeren van de CAD/CAM-restauraties werd in twee afzonderlijke sessies voltooid. Na het cementeren van alle indirecte restauraties werden directe veneer restauraties op maxillaire frontelementen gemaakt om de esthetiek te verbeteren.

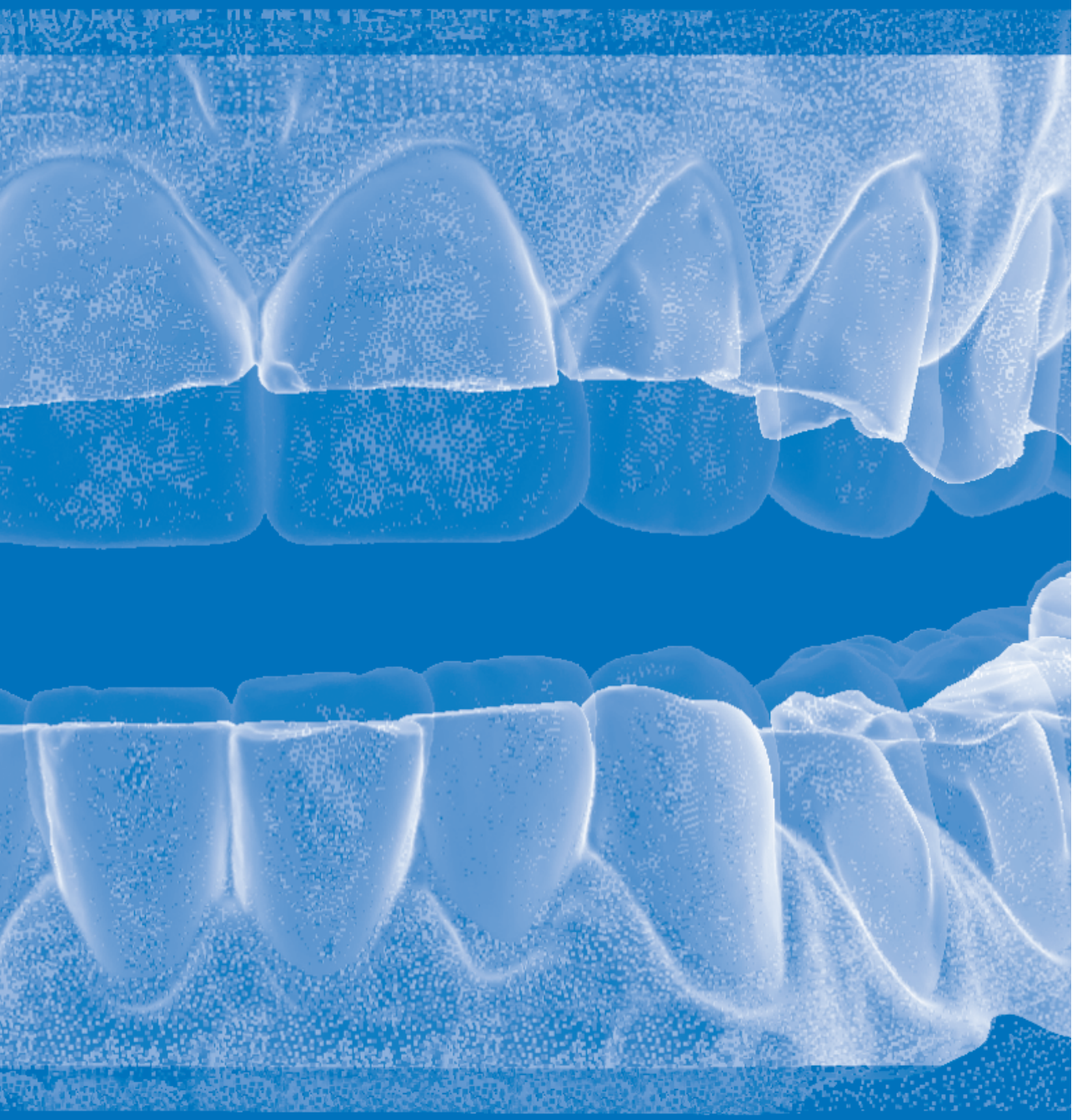
De volledig digitale workflow toonde een goed functioneel en esthetisch resultaat van de restauratieve behandeling. Er was echter geen informatie beschikbaar over het klinische succes op korte termijn van deze restauraties. Deze prospectieve studie wordt beschreven in **hoofdstuk 5**. Het doel was om de klinische prestatie van minimaal invasieve CAD/CAM nanokeramische restauraties te evalueren bij de restauratieve behandeling van gegeneraliseerde gebitsslijtage. De CAD/CAM-restauraties werden geplaatst op alle elementen en werden geëvalueerd op hun klinische aanvaardbaarheid na 1 maand en na 1 jaar. Voor de restauraties werden vergelijkbare faalniveaus gebruikt als beschreven in hoofdstuk 3. Daarnaast werd de OHRQoL beoordeeld op baseline en na 1 jaar. 21 Patiënten (leeftijd: 41,7 ± 10,4j) werden na 1 jaar geëvalueerd (13,5 ± 1,2m). Er werden 568 indirecte CAD/CAM-restauraties geplaatst. Geen enkele werd vervangen of ging verloren. 12 stuks werden gerepareerd en 10 gereviseerd. De succespercentages waren 100% tot 97,2%.

De restauratieve behandeling had een significant positief effect op de OHRQoL ($p<0,001$). Bovendien werden op baseline twee kenmerken van mechanische tandslijtage en drie kenmerken van chemische tandslijtage gescoord. De associatie tussen falen (breuk) van restauratie en de etiologie van tandslijtage werd geanalyseerd met een multilevel logistische regressieanalyse, met een 'random intercept' voor de patiënt. De aanwezigheid van 1 of 2 kenmerken van mechanische gebitsslijtage gaf geen significant verhoogd risico op mislukte restauraties ($p=0,78$). De aanwezigheid van 2 of 3 kenmerken van chemische gebitsslijtage, vergeleken met de afwezigheid van deze kenmerken, resulteerde in een significant lager risico op gefaalde restauraties ($p=0,002$).

Deze bevindingen tonen aan dat minimaal invasieve CAD/CAM nanokeramische restauraties op korte termijn bevredigend presteren. Andere prospectieve studies in het RTWP en de studie beschreven in hoofdstuk 3 toonden aanvaardbare klinische prestaties van directe composietrestauraties. Het is onduidelijk waarom de conventionele ICR, zoals beschreven in hoofdstuk 3, inferieur presteerden in vergelijking met de CAD/CAM-restauraties en de DCR. **Hoofdstuk 6** beschrijft een studie die tot doel had de klinische presentaties te reproduceren en te vertalen naar een *in vitro* opstelling om de mechanische eigenschappen te evalueren en deze te koppelen aan de klinische resultaten van de gebruikte materialen in de studies van de RTWP. Er werden dertig cilindrische samples (Ø12,0 mm, 1,2 mm dik) van vier composieten vervaardigd (Clearfil ™ AP-X (AP), Filtek ™ Supreme XTE (FS), Estenia ™ C&B (ES), en Lava Ultimate (LU)). Cyclische belasting (200N, 2 Hz) werd concentrisch toegepast op 15 samples per composiet met een ronde 'indenter' van speksteen (r=3.18 mm) in water in een cyclus van 'contact, druk, schuif en schuif terug' (10^5 cycli). Cyclische belasting resulteerde in slijtage op het oppervlak van de samples. Het slijtagelitteken werd geanalyseerd met behulp van profilometrie en virtuele berekening van het volume. Alle samples werden belast tot breuk in een biaxiale buigsterkte opstelling. Het effect van het materiaal op het volume van slijtage werd geëvalueerd met een regressieanalyse. Met AP als referentiegroep vertoonde FS een vergelijkbare mate van volumeverlies, maar beide indirecte composieten hadden een significant lager volumeverlies. De buigsterkte van de composiet samples werd geanalyseerd op het effect van het materiaal, het effect van de vermoeiingstest en de interactie tussen het materiaal en de vermoeiingstest. Met niet-vermoeide AP samples als referentiegroep hadden niet-vermoeide ES samples een vergelijkbare buigsterkte. FS en LU hadden een significant lagere buigsterkte dan AP. Alleen voor ES samples kon een interactie tussen de vermoeiingstest en het materiaal worden waargenomen ($p<0,001$; 95%CI: -96,1 - -54,6). Deze studie toonde aan dat ES een slechte vermoeiingsweerstand had en dat directe hybride en directe nanocomposieten een gelijke slijtvastheid hadden. De indirecte composieten vertoonden een betere slijtvastheid dan de direct verwerkte composieten. Deze resultaten komen overeen met de resultaten van klinische studies in het RTWP. De gebruikte laboratoriumtest kan als klinisch relevant worden beschouwd, aangezien de klinische presentaties in het laboratorium konden worden nagebootst. Bovendien is de eerste stap in de cyclus van translationeel onderzoek gezet met het nabootsen van klinische presentaties in het laboratorium; 'van de kliniek naar het laboratorium'.

Hoofdstuk 7 bespreekt de resultaten van de geïncludeerde studies en geeft aanbevelingen voor tandartsen. Verder bespreekt het richtingen voor verder onderzoek.

Het hoofddoel van dit proefschrift was het bestuderen van minimaal invasieve restauratieve behandelingsbenaderingen voor de behandeling van matige tot ernstige gebitsslijtage. Specifieke variabelen in de complexe behandeling van gesleten gebitselementen zijn bestudeerd. We kunnen concluderen dat het testen van de nieuwe VDO voorafgaand aan een restauratieve behandeling met een UV geen toegevoegde waarde heeft op de restauratieve behandeling. Directe composietrestauraties laten op middellange termijn klinisch aanvaardbare resultaten zien bij deze complexe rehabilitaties, alhoewel onderhoud door polijsten en incidentele reparaties nodig zijn. Conventionele indirecte composietrestauraties zijn niet geschikt in de posterieure regio. CAD/CAM-restauraties lijken een goed alternatief te zijn om een dentitie met gebitsslijtage op indirecte indirect te herstellen. Bovendien kunnen we concluderen dat het mogelijk was specifieke klinische resultaten van het RTWP na te bootsen in een laboratoriumopstelling. Het conventionele indirecte composiet vertoonde ook in de laboratoriumopstelling een slechte vermoeiingsweerstand. Dit zou een beslissende factor kunnen zijn in het matige klinische resultaat van de conventionele indirecte restauraties.



9

DATA MANAGEMENT PLAN

LIST OF PEER REVIEWED PUBLICATIONS

PHD PORTFOLIO

ACKNOWLEDGEMENTS

CURRICULUM VITAE

DATA MANAGEMENT PLAN

The studies presented in chapter 2, 3, 4, and 5 of this thesis are based on human studies, which were conducted in accordance with the principles of the Declaration of Helsinki. The medical and ethical review board committee on Research Involving Human Subjects Region Arnhem Nijmegen, Nijmegen, The Netherlands, has evaluated, prior to commencement of the studies, if approval of the committee was obligatory. For the two Randomized Controlled Trials (Chapter 2 and 3) such an approval was granted by the committee. For the prospective study described in chapter 4, the committee decided that their approval was not obligatory to conduct the study. The Standard Operating procedures (SOP's) of the studies are stored on the department's H-drive (H:\THKdata$\\umcfs012\ALG PCT\Eso\9-Promotietrajecten, diverse projecten\Luuk Crins).

The data obtained that was used for this thesis was archived according to the Findable, Accessible, Interoperable and Reusable (FAIR) principles. Patients received written informed consent when patients were esteemed eligible for inclusion. During all appointments (before treatment and all later recall appointments) patient received questionnaires on paper. Signed informed consent forms and completed questionnaires are stored in the departments' archive (Radboudumc, department of dentistry, 4th floor, room number: M362.04.422A). The paper data was also digitally stored using the FileMaker software (Castor was not yet available at the onset of the Radboud Tooth Wear Project in 2010). Data management and monitoring were also performed within FileMaker.

The digital database of FileMaker, that was used for the studies presented in chapters 2, 3, 4, and 5, is stored on the department's H-Drive: (H:\THKdata$\\umcffs012\ALF PCT\Eso\Data in Filemaker). To assure the participants' privacy, encrypted and unique individual subject's codes were used to handle the data. The codes correspond with the code on the patient- and dental professional's booklet. All data for the study presented in chapter 6 is stored on the Research Drive (umcsm36):\THK-RES$,202305).

The databases used for the statistical analysis and the computation code for the analysis (syntax) is stored on the department's H-drive (H:\THKdata$\\umcfs012\ALG PCT\Eso\9- Promotietrajecten, diverse projecten\Luuk Crins).

The data will be saved for 15 years after the termination of the study. Using these patient data in future research is only possible after a renewed permission by the patient as recorded in the informed consent.

LIST OF PEER REVIEWED PUBLICATIONS

Publications related to this thesis

Crins LAMJ, Opdam NJM, Kreulen CM, Bronkhorst EM, Huysmans MDNJM, Loomans BAC. Randomised controlled trial on testing an increased vertical dimension of occlusion prior to restorative treatment of tooth wear. J Oral Rehabil. 2023 Apr;50(4):267-275. doi: 10.1111/joor.13408.

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Kreulen CM, **Crins LAMJ**, Opdam NJM, Loomans BAC. Rehabilitation of Worn Dentition with CAD-CAM Restorations: A Case Report. J Adhes Dent. 2022 Apr 13;24(1):187-194. doi: 10.3290/j.jad.b2916447.

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Crins LAMJ, Opdam NJM, Huysmans MDNJM, Zhang Y, Loomans BAC. An in vitro evaluation of the fatigue behavior of resin composite materials as part of a translational research cycle. *In preparation*

Other publications

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Van Sambeek RMF, de Vos R, **Crins LAMJ**, Bronkhorst E, Mehta SB, Pereira-Cenci T, Loomans BAC. Perception of oral health related quality of life and orofacial aesthetics following restorative treatment of tooth wear: A five-year follow-up. J Dent. 2023 Sep;136:104626. doi: 10.1016/j.jdent.2023.104626. Epub 2023 Jul 19.

Mehta SB, Bronkhorst EM, Lima VP, **Crins L**, Bronkhorst H, Opdam NJM, Huysmans MDNJM, Loomans BAC. The effect of pre-treatment levels of tooth wear and the applied increase in the vertical dimension of occlusion (VDO) on the survival of direct resin composite restorations. J Dent. 2021 Aug; 111:103712. doi: 10.1016/j.jdent.2021.103712.

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PHD PORTFOLIO

Name PhD candidate:	Luuk A.M.J. Crins
Department:	Department of Dentistry
Graduate School:	Radboud Institute for Health Sciences
PhD period:	01 feb 2018 – 26 jan 2024
Promotors:	Prof. dr. Bas Loomans, Prof. dr. Marie-Charlotte Huysmans
Co-promotor:	dr. Niek Opdam

	Year(s)	ECTS
TRAINING ACTIVITIES		
a) Courses & Workshops		
Ernstige Gebitsslijtage: Diagnostiek en Behandeling	2017	0,6
De mondscanner, ook iets voor u?	2018	0,3
RIHS- Introduction course for PhD candidates	2018	0,5
RIHS PhD introduction course	2018	0,8
Biostatistics for PhD students at the department of dentistry	2018	1
Radboudumc – BROK course	2018	1,5
Functionele Opbouw van het Gebit bij Ernstige Slijtage en Tandboogonderbrekingen	2019	0,3
Hakman I – Psychodiagnostiek voor tandheelkundige specialismen	2019	0,6
Radboud Gebitsslijtage Klinische Module	2019	8,6
Radboudumc – Scientific Writing for PhD Candidates	2020	3
Radboudumc – Scientific Integrity	2020	1
Radboudumc – Over perfectionisme – sessies voor promovendi	2022	0,8
Hakman II – Psychodiagnostiek voor tandheelkundige specialismen	2022	0,6
Injection Moulding Technique	2023	0,3
b) Seminars & Lectures		
Research seminars at Department of Dentistry	2018-2023	2
Research seminars at faculty of dentistry of the New York University (NYU)	2019	0,2
c) Symposia & Congresses		
IADR General Assembly London	2018	1
TP gebitsslijtage	2018	0,3

Alumnidag	2018, 2019, 2020, 2022	1,2
ConsEURO Berlin	2019	0,9
Duch Dental Science Days (video interview)	2022	0,3
IADR-CED Marseille	2022	0,9

d) Other

Journal club	2019-2020	0,5
Audit of clinical study (Marjolein Bulthuis)	2022	0,5

TEACHING ACTIVITIES

e) Courses & Workshops

Management of Tooth Wear for Norwegian colleagues	2019	0,6
PAOT Course 'Functionele esthetiek of *Italiaanse* school	2021	0,6
PAOT teaching 'etsbruggen'	2022	0,3

f) Lecturing / Oral Presentations

IADR-CED Robert frank competition *(Honourable mention)*	2020	1
Oral Presentation Alumnidag	2022	1
Moderating webinar of PAOT (3x)	2022	0,5
Oral Presentation SCEM – Landelijke dag voor de preventieassistent	2022	0,5
Oral Presentation SCEM – conference for oral hygienists	2023	0,5
Oral Presentation for dentists in military service on the clinical management of tooth wear	2023	0,5
Oral Presentation Update of the Radboud Tooth Wear Project	2023	0,3
Oral Presentation for "Nederlandsch Tandheelkundig Genootschap"	2023	1
Webinar for 'Nederlands Tijdschrift Voor Tandheelkunde'	2023	1

g) Supervision of students

Jason Fokker - Master 5 & 6	2020-2023	1
Lilian Berenpas – Master 5 & 6	2021-2022	1
Romy Munniksma – Master 5 & 6	2021-2022	1
Janine Jeh – Master 6	2023	0,5
Narges Quaderdan – Master 6	2023	0,5

Total ECTC	39,5
Total hours	1106

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De Nederlandse Vereniging voor Gnathologie en Prothetische Tandheelkunde heeft bijgedragen aan de drukkosten van het proefschrfit.

CURRICULUM VITAE

Luuk Crins was born on November 21st, 1991, in Swartbroek, The Netherlands. In 2010, he started his dental education at the Radboud University and was selected to participate in the *Honours Programme*, an extracurricular project on academic research, during the last two years of the bachelor phase. He performed two research internships during his dental education at the Radboud University with internships at the Federal University of Pelotas (Brasil), in 2013 and the New York University (USA), in 2016. In April 2017, he graduated as a dentist at the Radboud University, receiving the degree of Master of Science.

From February 2018, Luuk worked as a part-time PhD-candidate at the department of Dentistry of the Radboud University (Radboudumc). In 2019, he returned to the New York University for a research internship to acquire data used in one of the studies in this thesis (Chapter 6). During the PhD-trajectory, he engaged in clinical activities at the clinic of the Radboud Tooth Wear Project to train himself in the clinical management of patients with tooth wear. The clinical activities ranged from data acquisition to the restorative treatment of patients with tooth wear. Luuk received the NVGPT publication award for best academic publication in the category primary research (*in vitro* and *in vivo)* in 2021 for the study described in chapter 3. He consecutively won that NVGPT publication award in 2022 for the study described in chapter 5.

After receiving the degree of Master of Science, Luuk started to work in several local dental practices. In addition to his appointment at the Radboud University, he currently works part-time as a general practitioner in a referral and group practice, where he focusses on adhesive and reconstructive dentistry of patients with tooth wear.