PROTOCOL: Cervical Localisation Code – validation of a new index

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1. Introduction

Tooth wear indices serve to capture and classify the severity of dental surface loss, for use in prevalence and incidence studies and management of the condition. Tooth wear can also be predictive of other oral conditions such as dentine hypersensitivity (DH), a common, painful oral condition which occurs when an area of dentine is exposed, usually at the cervical margin [1]. In addition, tooth wear often occurs in combination with gingival recession [2]. Ideally tooth wear indices could contribute to the diagnosis of DH and, with this is mind, it would be useful if the presence of a recession defect could be captured within the index.

There are numerous tooth wear indices published in the literature, yet the variety of their scoring criteria often renders the studies incomparable and has resulted in difficulties evaluating the overall status of the condition [3]. The Basic Erosive Wear Examination (BEWE) was introduced to overcome these problems, designed to be simple and easy for use by general dental practitioners, whilst also allowing re-analysis and integration of results from existing studies [4]. The aim was to prevent continued development of further indices after creation of an internationally accepted standard.

In 2011, a study was conducted across general dental practices and University teaching hospitals in Europe to investigate the relationship between DH, erosive tooth wear and periodontitis in the aetiology of non-carious cervical lesions [5],[6] The indices used to record tooth wear in this study included a BEWE severity code [4] modified to provide a separate score for each surface of the tooth, and a localisation code. The latter was designed to indicate the area of the tooth affected by tooth wear, yet its practical application was confusing as the codes could overlap in some clinical scenarios, leaving the score subject to examiner interpretation. In the absence of a mechanism to record localisation however, the BEWE severity code does not allow us to appreciate whether the scored tooth wear is localised occlusally/ incisally, or if it is focused in the cervical region. The severity score also lacks information on dentine exposure but rather focuses on the overall surface area of the tooth affected. This focus on surface area recognises that the distinction between lesions restricted to the enamel and dentine is difficult in the cervical region [7] yet, the presence of dentinal exposure is a requirement for the accurate diagnosis of DH. Given this limitation of BEWE, ten years after its introduction we propose the adoption of a new index: 'Cervical localisation code', designed specifically to assess tooth wear in the cervical region and its association with DH and gingival recession.

As the population are retaining their natural dentition for longer than previous generations, it is likely that tooth wear and gingival recession will become increasingly common problems [8]. Both of these conditions can lead to dentine exposure which, under the right circumstances, causes the initiation of DH - their common symptom. Our proposed Cervical localisation code has been designed to record exposure of radicular dentine (gingival recession) and tooth wear on the anatomical crown or root in the cervical region, recognising the multifactorial aetiology of dentine exposure which could lead to DH in this region. The index also includes a section which has been developed to provide the clinician with focused prevention and management strategies for each score.

The Cervical localisation code is deliberately simple, enabling it to be accessible to all practitioners in general dental practice and the descriptions have been designed to be reproducible under varying conditions- for example magnification, light and hydration state of the tooth. The index has been designed for use as both an epidemiological and clinical tool- highlighting the possible aetiology of any lesions and detailing how best to manage the individual patient's needs.

In the future, we hope that this index is adopted, alongside the BEWE, as a guide which focuses management of the cervical area in primary care dentistry. We intend to roll out its use in a future study involving foundation dentists working in general dental practices within the UK.

2. Principal aim and hypothesis

2.1 Principal aim

To validate our proposed clinical classification of the cervical region using three independent dentists to demonstrate inter and intra-examiner agreement.

2.2 Hypothesis

The four cervical localisation codes proposed (0-3) represent clinically distinguishable scenarios which can be scored reproducibly.

3. Experimental design and methodology

3.1 Type of study

The study is a cross-sectional observational, epidemiological validation study that will take place within the University of Bristol Dental Hospital. Study participants will be healthy dentate adult volunteers aged 18 or over, recruited from University Dental School/Hospital staff, students and patients. In addition, previous participants who have expressed interest in participating in new studies with the Clinical Trials Unit at the Bristol Dental School will also be approached. 39 healthy volunteers will be enrolled. Eligibility criteria are minimal as we intend to be as inclusive as possible.

Volunteers who provide informed consent to participate and fulfil the inclusion and exclusion criteria will undergo an identical clinical examination with each of the investigator dentists in turn. Three investigator dentists will be assigned for the course of the study, and each will independently score all participants. Each investigator dentist will have their own unique examiner ID by which their clinical scoring sheet will be identified. These examiner IDs will not be disclosed to the statistician. The investigator dentists will not be able to confer with one another to ensure that all scores are derived independently. In order to assess intra-examiner reliability, each investigator dentist will carry out a second examination once in every 3 patients, with an interval of approximately 30 minutes in between each examination. This will be scheduled so that only one investigator dentist repeats the second examination on an individual patient. Statistical analyses will be performed on the data to measure inter and intra examiner reliability.

It is also important that the dentist–patient relationship is maintained and that ongoing care of the patient is not affected by participation in the study.

3.2 Selection of participants

3.2.1 Recruitment

The study participants will be healthy dentate adult participants aged 18 or over, recruited from University Dental School/Hospital staff, students and patients. In addition, previous participants who have expressed an interest in participating in new studies with the Clinical Trials Unit at the Bristol Dental School will be approached. A record of all those approached will be retained, and the number approached and declined recorded.

3.2.2 Informed consent

For every person approached to be included in the study, the investigator/research dentist, or a designated member of the study team will:

- Provide the potential participant with an information sheet about the study
- Explain the study to the potential participant
- Answer any questions the potential participant has about the study
- Complete a consent form with participants who agree to take part in the study

The investigator/ research dentist will then assess inclusion and exclusion criteria following provision of written informed consent.

3.2.3 Inclusion criteria for participants

1. Healthy participants of either gender
2. Aged 18 or over
3. Understand and are willing, able and likely to comply with all study procedures and restrictions
4. Accept the form of the study and signs a declaration of informed consent
5. Have a minimum of 10 teeth not including implants or teeth with crowns or bridges

3.2.4 Exclusion criteria for participants

1. An employee and/or a family relative of the investigator dentists
2. Anyone who in the investigators opinion is not suitable to take part in the study

3.2.5 After enrolment onto the study

Participants who have consented to take part in the study and who fulfil the inclusion and exclusion criteria will undergo 4 identical clinical examinations performed independently by 3 investigator dentists. The participant's final examination will be performed by the same dentist as their first examination, approximately 30 minutes after the first clinical examination. No therapeutic procedures will occur between examinations.

3.2.6 Randomisation

Participants will be randomised by study staff equally to 3 treatment sequence groups using a block randomisation scheme. The 3 investigator dentists are to be labelled A, B and C. Thirteen of the 39 participants will be scored by the 3 dentists in the sequence A – B – C – A. Another 13 will be scored by the 3 dentists in the sequence B – C – A – B. The remaining 13 will be scored by the 3 dentists in the sequence C – A – B – C.

Examination Regimen	Investigator Dentist Order
1	A – B – C – A
2	B – C - A – B
3	C – A – B - C

3.2.7 Study duration

The study duration for each participant will be one appointment which will last between 30-60 minutes.

4. Data collection

Investigator and research dentists will recruit participants from patients attending an appointment at the Bristol Dental Hospital and Hospital staff and students. The participants will be those who have previously participated in a study and have expressed their interest in participating in future studies. Following consent, patients who agree to participate and are eligible to participate according to the inclusion and exclusion criteria will be admitted to the study. Each participant entered into the study will be allocated a unique participant identification number.

4.1 Clinical Examination

The clinical examination will involve capturing scores for the cervical localisation code on all eligible tooth surfaces, 7-7 both arches (buccal and palatal/lingual).

Dental exclusions:

- Missing teeth
- Teeth with gross caries
- Any tooth surface with crown or bridgework
- Any tooth surface with a fixed orthodontic appliance

- Any tooth surface with a large restoration/restoration in the proximity of the cementoenamel junction.

4.2 Clinical photographs

Each study dentist will request consent from all participants to take photographic images of their dentition when required. These images will be used when reviewing the differences between examiner scoring and to generate discussion of any differing interpretations of the code. The photographs will be identified by participant number and will only include an image of the oral area.

5. Data Management

All study data collected will be anonymous. Participants will be allocated a unique participant number on enrolment which will be recorded on the clinical form and any photographs taken. Data will be recorded on paper clinical forms and will be inputted manually onto an electronic spreadsheet by a member of the research team. No names, only a participant number, will be recorded against the data item in the electronic file created. This information will form the clinical data database. All anonymised data will be supplied to the study statistician (Prof Robert Newcombe) for analysis. The paper forms will be archived.

At the end of the study, the collected data will be analysed to establish the index reliability. The results will be combined with that of a coinciding European study, which involves recording the Cervical localisation code for 4900 patients. A report with statistical tables and conclusions will be prepared to establish the validity of the index. All participant information published will be anonymous.

5.1 Statistical analysis

All clinical scoring will be entered by clear professional data entry processes incorporating comprehensive checking such as double entry and validity/reality checks for each field, with missing values clearly identified. The data will be transferred to SPSS for analysis.

The 3 investigator dentists are to be labelled A, B and C. Thirteen of the 39 participants will be scored by the 3 dentists in the sequence A – B – C – A. Another 13 will be scored by the 3 dentists in the sequence B – C – A – B. The remaining 13 will be scored by the 3 dentists in the sequence C – A – B – C.

The ordered 4 point scale will be treated as numerical and parametric analyses used unless the data strongly indicates this is inappropriate. Both random and systematic variation between and within examiners will be quantified. Intra-examiner variation will be assessed by comparing the first and final scores. This will be done for all examiners together, and similar analyses will be considered for each examiner separately. Inter-examiner variation will be assessed by comparing the 1^{st}, 2^{nd} and 3^{rd} scores in a two-way analysis of variance model; pairwise differences between examiners will also be considered.

Analysis will be performed for individual tooth positions and whole-mouth maximum scores. Similar analyses based on all participating teeth (up to 39×28 i.e. 1092 teeth) will also be considered but will be interpreted with caution because independence should not be assumed.

The intra-observer variation for any tooth site or for the whole mouth maximum score will be quantified by a standard deviation estimate s which has 39 degrees of freedom. The 95% confidence interval for s runs from 0.819s to 1.284s. Thus this study size enables estimation of within-observer variation as being between 18.1% lower than and 28.4% greater than the point estimate.

6. Reporting Adverse Events and Serious Adverse Events

All AEs will be reported from the time a signed and dated informed consent form is obtained until completion of the last study-related procedure. Those occurrences meeting the definition of SAEs must be reported using the UH Bristol Serious Adverse Event Form, including SAEs spontaneously reported to the Investigator within 30 days after the participant has completed the study (including post study follow-up). UH Bristol, on behalf of the Sponsor, will evaluate any safety information that is spontaneously reported by a CI beyond the time frame specified in the protocol.

All AEs, regardless of seriousness, severity, or presumed relationship to study treatments, must be recorded in the source document and the CRF, together with any measures taken. CIs must record in the CRF their opinion concerning the relationship of the adverse event to study therapy. UH Bristol, on behalf of the Sponsor, assumes responsibility for appropriate reporting of adverse events to the regulatory authorities.

AEs will be recorded in the AE section of the CRF.

All SAEs must be reported to the UH Bristol contact (0117 3420233) by investigational staff within 24 hours of their knowledge of the event.

6.1 Follow-up of adverse events and serious adverse events

After the initial report, the investigator is required to proactively follow up with each participant and provide further information on the participant's condition. All AEs/SAEs will be followed until resolution, until the condition stabilizes, until the event is otherwise explained, or until the participant is lost to follow-up. The investigator may be required to obtain additional laboratory tests or investigations, and/or provide the University of Bristol with additional documentation, including autopsy reports.

7. **Research Governance**

7.1 Sponsorship

The Sponsor is the University of Bristol.

7.2 Ethical considerations

The Principal Investigator will ensure that this study is conducted in full conformance with the laws and regulations of the country in which the research is conducted and the Declaration of Helsinki.

7.3 Informed Consent

It is the responsibility of the investigator, or designee, to obtain written (signed and dated by the participant) informed consent from each individual participating in this study.

7.4 Independent Ethics Committee

This study has been reviewed and given favourable opinion by London – Queen Square Research Ethics Committee and the HRA. Any amendments will be reviewed by the Sponsor prior to submission for approval by the HRA and NHS Research Ethics Committee. We are applying for HRA and Ethics approval using the online Integrated Research Application System (IRAS).

7.5 Monitoring of the study

The University of Bristol has a policy for monitoring 10% of studies. Monitoring of studies is conducted in accordance with UH Bristol monitoring policy in relation to the service level agreement with the University of Bristol.

8. References

[1] M. Addy, P. Mostafa, R. Newcombe, Dentine hypersensitivity: the distribution of recession, sensitivity and plaque, Journal of Dentistry 15(6) (1987) 242-248.
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