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Intraoral scanner featuring transillumination for proximal caries detection. An in vitro validation study on permanent posterior teeth

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A R T I C L E   I N F O

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A B S T R A C T

Objectives: To assess the validity of an intraoral scanner system featuring near-infrared (NIR) transillumination to aid the detection of proximal caries lesions, and to compare the diagnostic performance of this system with that of conventional caries detection methods and with that of an intraoral camera featuring NIR transillumination (DIAGNOcam).

Methods: Ninety-five permanent posterior teeth were examined using a prototype tip functioning with TRIOS 4 intraoral scanner system (3Shape TRIOS A/S, Denmark) and emitting NIR light, DIAGNOcam, and visual and radiographic examination employing ICDAS criteria. One or two approximal surfaces per tooth, sound or with caries lesions at different stages, were examined (N = 158). Histological assessment was used as the reference standard.

Results: All methods showed excellent intra-examiner reliability (κ_intra ≥ 0.80). Two independent examiners assessed the NIR images obtained with both devices. The first examiner, who obtained and assessed the images, showed improved diagnostic performance than the second examiner, who only had access to the images. The inter-examiner agreement between the two examiners assessing the NIR images was substantial (κ_inter 0.57-0.72). The intraoral scanner and DIAGNOcam showed similar diagnostic performance. Regarding initial caries lesions, the NIR image assessment resulted in equal or improved sensitivity (SE 0.50-0.89) compared to radiographic assessment (SE 0.49-0.51) and higher than visual examination (SE 0.28-0.39). Radiographic and NIR image assessment resulted in similar SE in detecting moderate-extensive dentin caries lesions (SE 0.59-0.70), while visual examination showed an inferior value (SE 0.30).

Conclusions: The intraoral scanner system featuring NIR transillumination and DIAGNOcam showed an overall good diagnostic performance. The conventional caries detection methods showed inferior sensitivity at initial caries lesion stages. Clinical significance: Considering the promising diagnostic performance of the intraoral scanner featuring transillumination and the advantages offered by combining the NIR images with the 3D models of the teeth, this system has the potential to contribute towards more reliable caries detection and monitoring in clinical practice without the use of ionizing radiation.

1. Introduction

This paper’s novelty lies in investigating potential proximal caries detection using an intraoral scanner system featuring near-infrared (NIR) transillumination. The use of three-dimensional (3D) intraoral scanners for monitoring oral health, in particular for detection and subsequent observation of caries lesions, is increasingly receiving attention from researchers and industry [1–4]. NIR transillumination...
method has widely been investigated in the literature, mainly for the detection of proximal and occlusal caries lesions [5–10].

When NIR transillumination is employed for proximal caries detection, NIR light is emitted directly on the buccal and lingual gingiva of the examined teeth; the light transmitted through the gingiva, alveolar bone and dental tissues is received by a camera viewing the teeth from the occlusal surface [10–12]. During live imaging or on captured images, the sound enamel appears light grey, as the NIR light is transmitted easily through this tissue, while dentin and demineralized tissue, which scatter more light, appear dark grey [13–16].

Different NIR wavelengths have been investigated in search of the best image quality for clinical application, according to criteria such as good contrast between sound and demineralized dental tissue, high tissue penetration, and decreased light scattering [14–18]. Wavelengths within the range of 830–1310 nm have shown improved image contrast between caries lesions and sound dental hard tissues [15]. The commercial device that currently utilizes NIR transillumination (DIAG-Nocam, KaVo, Germany/CariVu, DEXIS, USA) [9], as well as prototypes used for research purposes [19], employ laser light at 780 nm, showing promising diagnostic performance for detection of proximal caries lesions. More specifically, pooled sensitivity of 0.97 and specificity of 0.91, which are superior to values observed for conventional caries detection methods, are reported by a recent systematic review [10]. However, the observed increased number of false-positive enamel lesions added to the challenge in determining the exact lesion depth and progression of dentin lesions are the main limitations of NIR transillumination [6,10,20]. Additionally, a particular matter observed when using DIAGNocam is the low signal-to-noise ratio on the images, either due to laser speckles or the presence of under/overexposed areas [7,19]. These areas usually correspond either to different materials present in the oral cavity, or to direct light reflection into the camera sensor, the latter resulting from suboptimal shielding of the light reflected from the surfaces and not coupled into the tissues. Another general challenge related to the application of NIR transillumination for monitoring caries lesions is the difficulty in obtaining subsequent 2D images with the same angle and relative position of the camera with respect to the examined tooth surfaces. This can possibly influence the apparent size of the caries lesion visualized on the NIR image.

Efforts were made in the prototype used in this study to reduce the noise observed on the NIR images compared to the existing commercial device: i) by eliminating laser speckles using light from light-emitting diodes (LEDs) instead of coherent laser light and ii) by employing a new design targeting to improve the adaptation of the NIR tip to the oral tissues and thus reduce over-exposed areas due to directly reflected light. Other improvements in the proposed prototype that could lead to enhanced image quality are the use of a different wavelength (850 nm), and the larger field of view.

Finally, by combining NIR to intraoral scanning, the exact position where each NIR image is taken is registered onto the 3D model of the teeth. This is expected to facilitate future acquisition of comparable images on the same positions, and potentially advanced and more objective monitoring of caries lesions.

This in vitro study aims to assess the validity of an intraoral scanner prototype featuring NIR transillumination to aid the detection and classification of proximal caries lesions. A further aim is to compare the performance of this device with that of standard caries detection methods (visual/radiographic) and a commercially-available intraoral camera (DIAGNocam).

2. Materials and methods

Four independent caries detection methods were assessed as index tests in this in vitro study:

- Intraoral scanner, featuring NIR transillumination imaging (TRIOS 4 intraoral scanner and prototype tip, 3Shape TRIOS A/S, Denmark);
- Intraoral camera, featuring NIR transillumination imaging (DIAGNOCam 2170U, KaVo, Germany);
- Visual examination, using the International Caries Detection and Assessment System (ICDAS) criteria for proximal caries lesions; and
- Radiographic assessment using the ICDAS criteria.

Histological assessment was used as a reference test. An overview of the methods is presented in Fig. 1, and the scoring systems used for the different index tests are provided in Table 1 and Supplementary Table S1.

2.1. Sample selection and preparation

Human permanent molars (n = 68) and premolars (n = 29), sound or with proximal caries lesions of different severity stages, were selected from a pool of extracted teeth stored in chloramine-T trihydrate aqueous solution (0.5% w/v). The teeth were selected based on a preliminary visual assessment to reach a balanced distribution of the different caries severity stages in the sample (40% sound, 30% with crown reconstructions, fractures, severe developmental defects, and extensive caries lesions on the occlusal, buccal, or lingual surfaces interfering with the approximal surfaces, were excluded. All teeth were extracted for therapeutic reasons by dental practitioners and donated to the University of Copenhagen, Denmark. As the teeth were anonymous leftover biological material, no approval by the National Ethical Committee was required. Description of sample size calculation is provided in Appendix pp.2.

The teeth were mounted in a visible light-cured resin base (Triad® VLC, DENTSPLY International, USA), which has similar optical properties to the tooth-supporting tissues [21]. The resin was applied to cover the roots of the teeth and was levelled at the cement-enamel junction, thus resembling the anatomy of the natural gingiva. The teeth were mounted as closely as possible to the in vivo scenario (Fig. 1): the approximal surfaces were mounted adjacent to each other, and close contact was established between neighbouring teeth. Twenty-one models of shortened artificial dental arches, consisting of four to six teeth either from the upper or lower jaw, were prepared. Fifteen of these models included both molars and premolars with a neighbouring canine; six models included only molars. The teeth were kept humid during the whole experiment.

2.2. Index tests

All teeth were first assessed using the intraoral scanner and camera featuring NIR transillumination. Imaging with both devices was conducted by the same operator (S.M.), on the same day, and under the same environmental light conditions. Only the approximal surfaces of premolars and molars in contact with a neighbouring tooth were assessed, in total 167 examination sites. Radiographic and visual assessments were conducted afterwards.

2.3. Intraoral scanner and camera featuring NIR transillumination

TRIOS 4 intraoral scanner and the prototype tip featuring NIR (Fig. 2) were supported by customized software (3Shape A/S, Denmark). Using this system, the teeth were first scanned with white light using a standard tip to generate 3D models. Subsequently, NIR images were obtained using the prototype tip.

DIAGNOCam (Fig. 1) has been described in previous articles [5,9]. In this study, the dedicated software (KaVo DIAGNOCam version 3.0.1, KaVo, Germany) was used for image acquisition and analysis.

To obtain NIR images, both devices were positioned parallel to the occlusal surfaces of the teeth, with the device arms in contact with the cervical tooth area and just apically to the level of the artificial gingival margin (Fig. 2). NIR light was emitted from each device’s light source.
directly onto the artificial gingiva. The light was transmitted through the resin base and the teeth, and received by a sensor in the devices.

2.4. NIR image assessment

Both devices allowed live imaging of the teeth and acquisition of NIR images in automatically-adjusted focus. For TRIOS 4, the plane of focus was automatically adjusted on the occlusal surface of the teeth, and the obtained images were subsequently aligned on the 3D models of the teeth.

Multiple NIR images with slightly different acquisition angles were obtained until at least one clear image of each examined surface was obtained, i.e. good contrast between enamel and dentin, minimal presence of overexposed areas and with the examined surfaces in focus. Classification of the proximal surfaces on the NIR images was first performed by S.M., who obtained the images using both NIR devices. Afterwards, a second examiner (A.R.) assessed these saved images on the examination sites marked by S.M.. The caries classification system used for the NIR image assessment is presented in Table 1 [19].

The NIR image assessments were conducted on each device’s respective software. Both software allowed adjustments of brightness and contrast on the NIR images, but the TRIOS software supported gamma adjustments too. The abovementioned adjustments were made according to each examiner’s judgement.

2.5. Visual examination

A third independent examiner (K.E.) assessed visually all approximal surfaces of the teeth while mounted on the shortened artificial dental arches. ICDAS criteria were employed (Supplementary Table S1) [22, 23]. All examinations took place in the same room with standardized illumination and aided by air drying.

2.6. Radiographs

Digital radiographs of the teeth were obtained by buccolingual X-ray irradiation (X-ray device SOREDEX, MINRAY®, exposure time 0.25 s, 60 kV, 7mA; Image plates VistaScan; Image plate scanner VistaScan Mini View, Dürr Dental). A fourth independent examiner (A.B.) used the ICDAS radiographic scoring system to assess each approximal surface on the radiographs. Examination of radiographs was conducted in a dark room and on an X-ray-calibrated screen (Table 1, Supplementary Table S1).

2.7. Reference test - histology

After all index tests, the teeth were separated from the model base using a cutting machine (Accutom, Struers A/S, Denmark) and a diamond disc (thickness ~0.4 mm, Buehler, Illinois). The proximal examination sites were photographed using a stereomicroscope (SteREO Discovery V8, ZEISS, Germany) under 1x optical magnification. Thereafter, S.M. defined 1-2 mesiodistal cutting lines on the teeth; these lines were positioned closest to the most severe point of the caries lesion. In the case of visually sound approximal surfaces, the cutting line was placed mid-sagittally. The teeth were then cut along their long axes using the abovementioned machine.

Tooth sections (Fig. 1) were manually ground using silicon carbide abrasive paper (grit no. 1000, Struers A/S, Denmark) until the maximum depth of the lesion could be confirmed. This step was skipped in case of obviously-sound surfaces or caries lesions into the inner third of the dentin. The tooth sections were photographed on the stereomicroscope (1.58x optical magnification) before and after gradual grinding. After measuring the lesion depth in relation to the corresponding thickness of the dental hard tissues on the photographs, a histological score was given to each approximal surface (Table 1). All measurements were taken using software (DeltaPix InSight V 5.2.6, DeltaPix, Denmark) and

![Fig. 1. Methods overview. The figure presents the different index tests assessed in the study (visual, radiographic, and NIR transillumination using intraoral scanner tip prototype or DIAGNOcam) and the reference test (histology). For the devices featuring NIR transillumination, the images on the left show the tip positioned on the examination model. Images a1 and b1 represent histological sections of the same tooth after semi-sectioning and images a2, a3, a4, b2 represent images of the same sections after gradual manual grinding. On the measurement image, L1 corresponds to caries lesion depth and L2 to enamel thickness.](image-url)
Table 1
The caries scoring system used for the NIR image assessments and representative images obtained with intraoral scanner and DIAGNOcam are presented in accordance to each histological level. Radiographs of the same teeth are also presented.

<table>
<thead>
<tr>
<th>Histological score</th>
<th>NIR caries score</th>
<th>3D Intraoral Scanner</th>
<th>DIAGNOcam</th>
<th>Radiographs</th>
</tr>
</thead>
<tbody>
<tr>
<td>E0</td>
<td>NIR0</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
<tr>
<td>Sound</td>
<td>No tooth decay. No dark grey area visible in approximal surface.</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
<tr>
<td>E1</td>
<td>NIR1</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
<tr>
<td>Caries in the outer half of enamel</td>
<td>Caries limited to enamel without any contact to DEJ</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
<tr>
<td>E2</td>
<td>NIR2</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
<tr>
<td>Caries in the inner half of enamel including DEJ</td>
<td>Enamel caries with single-point contact to the DEJ</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
<tr>
<td>D1</td>
<td>NIR3</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
<tr>
<td>Caries in the outer third of dentin</td>
<td>Enamel caries with extensive contact to the DEJ</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
<tr>
<td>D2 – D3</td>
<td>NIR4</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
<tr>
<td>Caries in the middle and inner thirds of dentin, with or without pulp involvement</td>
<td>Caries visible in dentin</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
</tbody>
</table>

DEJ, dentin-enamel junction.
Focus and brightness was adjusted on these NIR images from both devices according to main author’s judgement.
The radiographs were cropped around the area of interest.
Fig. 2. 3D intraoral scanner system featuring NIR transillumination. i) Prototype tip featuring NIR transillumination mounted on TRIOS 4 intraoral scanner. The tip (ii, iii) consists of a stiff part (white) and two black soft, flexible arms (b) which adjust their shape to the teeth and gingiva. LED light sources (a) emit light (wavelength 850 nm).

without staining.

2.8. Examiner reliability, blinding and calibration

All index test assessments were repeated twice by each examiner with a minimum interval of two weeks to evaluate intra-examiner reliability (κintra). The second assessments were conducted on randomly selected models constituting half of the sample (N₂ = 82 examination sites).

Inter-examiner reliability (κinter) associated with the NIR image assessments performed by the two independent examiners (S.M., A.R.) was also calculated.

Information about the researchers’ blinding, training and calibration are provided in the Appendix.

2.9. Data analysis

Weighted Cohen’s Kappa coefficients were used to assess κintra for all methods and κinter for the NIR devices.

Spearman’s correlation coefficient (r_s) was used to assess the correlation between the histological scores and the scores from each index test.

Sensitivity (SE), specificity (SP), positive (PPV) and negative predictive values (NPV), and diagnostic accuracy (ACC) were calculated from contingency tables using histology as reference. For these calculations, the cut-offs were set above each histological level (E1-D2 according to Table 1). The sample was dichotomized, and all lesions at histological levels beyond each cut-off were considered as positives and those prior to the cut-off as negatives. Accordingly, diagnostic accuracy measures were calculated for the following histological levels and their corresponding index tests scores: E1 (NIR1, ICDAS1, RA1); E2 (NIR2, ICDAS2, RA2); D1 (NIR3, RA3); and D2-D3 (NIR4, ICDAS3-6, RA4-6). No separate calculation was conducted at level D3, as no score distinguishing D2 and D3 lesions is defined for the NIR method. Similarly, no values were calculated for the visual assessment at the D1 level, as there is no visual ICDAS score reliably differentiating lesions located in E2 and D1 histological levels. The area under the receiver operating characteristic (ROC) curve was also calculated at the abovementioned cut-offs. The areas under the ROC curves (Az) for the index tests at the E1, E2, D1 and D2 levels were compared pairwise using DeLong’s algorithm [24], while SE and SP values were compared using McNemar’s test [25].

The analyses were conducted using IBM SPSS Statistics (Version 25, IBM Corporation), MedCalc statistical software (Version 19.6.4, MedCalc Software Ltd, Belgium), and Excel (2016, Microsoft corporation) with the level of confidence set at 95%.

3. Results

Out of the 167 examination surfaces initially included in the study, nine were excluded from the statistical analyses due to the following reasons:

- The resin material used as artificial gingiva had entered the examined proximal cavity and affected the lesion’s optical properties;
- the tooth broke while cutting and histological assessment was not possible; or
- there were defects on the approximal surfaces introduced by extraction instruments, only noted during the histological assessment.

Surfaces the examiners could not assess, i.e. unclear images, were considered as missing values. Thus, the final number of teeth included in the statistical analyses was 95 (66 molars, 29 premolars), with 158 examinations surfaces (N₁: N_molar = 101, N_premolar = 57).

Descriptive results for all methods for the first assessment are provided in Table 2 and Fig. 3. Contingency tables for each index test and ROC curves are provided in the Supplementary Table S2 and Supplementary Fig. S1, respectively.

All methods showed excellent intra-examiner reliability (κintra > 0.80). Moderate to substantial inter-examiner reliability (κinter 0.57-0.72) was observed for the NIR devices; the values for DIAGNOCam were marginally higher than those for the intraoral scanner. Both NIR devices showed at least similar (examiner A.R., r_s 0.52-0.61) or higher correlation with histology (examiner S.M., r_s 0.71-0.78) than radiographs (r_s 0.55-0.58). The visual assessment resulted in the lowest correlation with histology (r_s 0.42-0.43).

The two devices featuring NIR showed similar performance (Table 2) at all histological levels. At E1, E2 and D1 histological levels, the NIR devices showed overall higher Az, SE and ACC values than the visual and radiographic assessments. However, the NIR image assessment conducted by the second examiner (A.R.) resulted in lower Az, SE and ACC values than the assessment conducted by the first examiner (S.M.). Radiographic and visual assessments showed the highest SP values at E1 and D1 histological levels. When assessing the extensive caries lesions in the middle-inner third of dentin, no differences were identified between the radiographic and NIR image assessment. The visual assessment presented the significantly smallest area under the ROC curve (Az) with a subsequent impact on the SE at all histological levels.

4. Discussion

Using the 3D intraoral scanner system featuring NIR transillumination, it was possible to detect and classify proximal caries lesions. The current study results are in general agreement with the literature and confirm that, as regards the detection of initial caries lesions in enamel and dentin, NIR transillumination constitutes a reliable non-ionizing alternative, with equal or improved SE compared to radiographic and visual assessments [6,10,20,21]. Two clinically-important advantages of NIR transillumination are that (a) this method is more likely to identify initial caries lesions, where preventive approaches are possible, and (b) there is no overlap of the proximal surfaces of neighboring teeth on NIR images, which is frequently observed on bitewing radiographs. The latter may result in overlooking initial caries lesions or need for repetition of radiographs [11].

Nevertheless, identification of caries lesions on the NIR images, in particular initial lesions, depends on the angle of the incident light, which, together with the presence of anatomical characteristics or developmental defects, might increase the number of false-positive and/or false-negative results [20]. The above factors, together with the camera angulation, the NIR image settings, and the exact occluso-gingival location of the approximal caries lesions affect the
lesions’ visualization on the 2D NIR images. Thus, it becomes challenging - if not impossible - to distinguish between caries lesions located in the outer half of enamel from those in the inner half of enamel, or yet between lesions extending into the outer third of dentin and more profound lesions in the dentin. This explains the relatively low SE values observed for the NIR method at the E2 and D2 levels (Table 2). For this reason, and as the pulp is not visualized on the NIR images, assessing and monitoring more extensive dentin caries lesions and their proximity to the pulp is limited using NIR transillumination.

Although the prototype intraoral scanner system featuring NIR transillumination and the commercial devices are not ready to completely replace radiographs in dental practice, they could be applicable to supplement visual inspection reliably. In general, NIR transillumination can aid the detection of initial and more advanced caries lesions in the dentin. This explains the relatively low SE values between lesions extending into the outer third of dentin and more profound lesions in the outer half of enamel from those in the inner half of enamel, or yet in the outer half of enamel from those in the inner half of enamel, or yet between lesions extending into the outer third of dentin and more profound lesions in the dentin. This explains the relatively low SE values observed for the NIR method at the E2 and D2 levels (Table 2). For this reason, and as the pulp is not visualized on the NIR images, assessing and monitoring more extensive dentin caries lesions and their proximity to the pulp is limited using NIR transillumination.

Additionally, we speculate that blind assessment of NIR images, as conducted in this study without allowing the clinical tooth inspection, could, to an extent, have limited the diagnostic performance of this method from reaching excellent levels. We expect that in clinical practice, where both live NIR imaging and 2D NIR images can be used as an adjunct to the visual inspection of the teeth, some of the false-positive/negative results related to the mentioned characteristics (e.g. developmental defects, demineralization on nearby surfaces) could be avoided.

As the focus of this study was to investigate the diagnostic performance of the intraoral scanner featuring NIR transillumination, two examiners assessed the NIR images (SM, AR). Consequently, discrepancies between examiners assessing the NIR images and the inter-examiner reliability could be investigated for this method. The first examiner (S.M.) showed improved SE and Az compared to the second examiner (A.R.). S.M. had comparatively more experience with NIR transillumination, and was the one who operated the devices and obtained the images. A.R. received training and calibration before the experiment and had access only to the NIR images obtained by S.M. Regarding the conventional methods, their performance is widely...
investigated in the literature: a substantial level of reproducibility and accuracy is reported when trained and calibrated examiners employ the ICDAS criteria, as in the current study [27]. It is worth highlighting that the two examiners, KE and AB, are experts in the field of Cariology and have many years of experience with the ICDAS criteria. Significant discrepancies in the results could have been observed if more examiners with a shorter experience in Cariology research or general practitioners had also conducted the examinations [28]. When comparing the operation of the two NIR devices, both faster acquisition of acceptable images with larger field of view and less noise on the images were noted for the intraoral scanner. This, however, did not improve the scanner’s diagnostic capability; the prototype system showed an overall similar diagnostic performance to DIAGNOcam when considering the same examiner; an exception was noted for the second examiner’s (AR) sensitivity at the first caries stage (≥ E1) (Table 2).

Our findings encourage further development of the intraoral scanner system featuring NIR transillumination. Potential improvements lie in the automated alignment of subsequent NIR images on the 3D models, aiming towards accurate monitoring of caries lesions, or future development of an automated caries detection system based on machine learning [29]. Such improvements to the NIR scanner system might make this method less subjective and more reliable. Building upon the results from this study, further research is required to support the development of this NIR scanner system, to assess its performance in vivo, and to validate its ability to monitor early caries lesions.

5. Conclusion

The 3D intraoral scanner system featuring NIR transillumination for proximal caries detection showed an overall good diagnostic performance. Regarding the diagnostic accuracy and reliability, no notable difference between the intraoral scanner and DIAGNOcam was observed, while the conventional caries detection methods showed inferior sensitivity, particularly at the initial caries lesion stages.

Devices featuring NIR transillumination can complement the visual examination when detecting and monitoring initial proximal caries lesions as an alternative to the use of ionizing radiation. Considering the in vitro character of this study, further in vivo investigation is needed to assess the clinical performance of this intraoral scanner system featuring NIR transillumination.

CRediT authorship contribution statement

Stavroula Michou: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Writing – original draft, Visualization, Project administration, Funding acquisition. Christoph Vannahme: Conceptualization, Software, Resources, Writing – review & editing, Supervision, Funding acquisition. Azam Bakhshandeh: Conceptualization, Investigation, Resources, Writing – review & editing, Supervision, Funding acquisition. Kim R. Ekstrand: Conceptualization, Investigation, Writing – review & editing, Supervision, Funding acquisition. Ana R. Benetti: Conceptualization, Investigation, Resources, Writing – review & editing, Supervision, Funding acquisition.

Declaration of Interest

The authors declare that the first author (SM) is employed at 3Shape TRIOS A/S and her salary is partially covered by Innovation Fund Denmark. The co-author CV is also employed at 3Shape TRIOS A/S. The authors AB, ARB and KE declare no conflict of interest.
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Supplementary materials

References