SMART composite (Self-bonding Material for Atraumatic Restorative Treatment) restoration of children's primary molar teeth after minimal caries removal: Class IIa device in a single site, single arm study. Stage 1 Assessment of Safety

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Clinical trial number 228909

- Aims and objectives:

The primary aim of this clinical trial was to monitor for any adverse events and evaluate the safety of using SMART composite to restore primary teeth that were indicated for extraction. As a secondary objective, these teeth were also used upon extraction to evaluate retention of restorations and placement procedure. Furthermore, tooth sectioning was employed to determine whether the SMART composite was able to penetrate and seal carious dentine under highly challenging conditions.

- Introduction:

Following the Global Minamata agreement amalgam dental restorations are being phased out. Whilst cements are too weak for larger cavities, the complexity of placement of conventional dental composites makes them unsuitable for young children. Tooth extraction is then often the only clinical option. This report describes a first-in-human safety study of a new composite that has the potential to address this problem.

The SMART composite has been designed to be placed without need for isolation from saliva via a rubber dam. It has the potential to be placed without anaesthetic, drill, etch, rinse, prime, bond and multiple composite layering and light exposure steps required with conventional composite placement. Instead it can be placed following minimal removal of only the soft surface highly infected dentine. The SMART composite paste may be injected in one go from a single use compule directly onto underlying dentine affected by caries. Exposure of the composite surface to a blue dental light then solidifies the paste within the tooth structure restoring the tooth to its original shape, appearance, mechanical properties and function.

In the described clinical trial, the restorative material paste was placed as a temporary filling in primary teeth due for extraction. The trial design has minimised risk, improved comfort for the trial patients whilst waiting for their extraction appointment, but in addition allowed examination of the extracted teeth in a laboratory. This enabled investigation of the restorations at high magnification. It has also allowed sectioning to assess if long resin tags form under clinical conditions. These are important to halt disease progression, mechanically stabilise diseased dentine and aid SMART composite bonding.

- Materials and methods:

SMART composite in compules (stored at 4ºC) were used for the clinical trial. SMART composite was mixed (lot number 782332) in Nov. 2017 and packaged in individual compules (Lot No. 783139) in March 2018 (Manufacturer – Davis, Schottlander and Davis Ltd.). Colorimetric, spectroscopic, mechanical, cytotoxicity and carcinogenicity testing (described in other reports) were employed to ensure continuing paste stability and safety during the trial.

Patients were recruited between January and June 2019 (n=7). Each patient had one primary molar (first or second, of ICDAS score 5 or 6) slightly excavated to remove the soft highly infected caries (Atraumatic Restorative Technique, ART). It was then restored with SMART composite (by Prof Paul Ashley) in a single-step without the use of etch and bond. The restorations were light-cured for 40s.

All restorations were in the mouth for at least one month during which, adverse events were assessed immediately during placement, at 3 days (via telephone call) and at the extraction appointment.

Extracted teeth were collected, cleaned and soaked in 1% Chloramine T for 3 days for disinfection then stored at 4ºC in water until evaluation in the lab. Periapical X-rays were obtained using a Planmeca Prox machine (Planmeca Oy, Helsinki, Finland) with the following settings: 70kV and 8mA for 0.1s. Teeth were x-rayed from the buccal side and imaged using a digital camera (Canon EOS 1300D) and a Nikon lens (AF Micro Nikkor, 55mm).

Two teeth were ground down mesiodistally parallel to the long axis of the tooth from the buccal side using abrasive paper (grit no 220). When the adhesion interface was exposed, Rhodamine B (0.2% in isopropanol) was applied for 2 minutes then gently rinsed. Confocal laser Scanning microscopy (CLSM) was subsequently used to scan the interface using an oil objective lens (x60) and the Z motor to scan different levels. Acquired scans were analysed using ImageJ software package.

- **Results and Discussion**

Summary

Seven patients were recruited in total as per CIP. Six patients completed the trial and one withdrew after restoration placement. There were two protocol violations where for reasons unrelated to the SMART material extraction of the tooth was delayed. No adverse reactions were reported. Patient demographics were - 2 female, 5 males. Mean age 8 years. The first restoration was placed 22/1/19.

The restorations were placed as an interim solution to restore function of the tooth until extracted. Each patient received one restoration. Restoration placement procedure was rapid (1-2 minutes) and simple (single step) and well accepted by patients.

Adverse effects:

Following immediate evaluation after restoration placement and the evaluation at 3 days and at the extraction appointment, no adverse effects as described in the CIP were reported. No pain was reported in relation to the restored teeth despite all cavities being deep and close to the pulp.

Protocol violations:

All patients were assigned a planned extraction appointment one month after restoration placement. However, patient 3 had the tooth extracted on 22nd May instead of 20th March due to issues unrelated to the SMART filling placement (see trial deviation letter dated 28th May). Furthermore, patient 4 had their tooth removed on the 12th instead of the 5th of April due to the patient being unable to attend their first scheduled appointment (see trial deviation letter dated 7th May). Patient 6 also decided to withdraw from the trial after material placement and did not want the filled tooth to be extracted. This patient is being kept under review during follow up appointments until tooth exfoliation. They are not reporting any pain or problems with this tooth

Imaging extracted teeth:

Representative images of the teeth upon extraction and the related dental X-rays are shown in Figure 1 below. Remaining images are provided in appendix A.

SMART composite restorations were always detected in the cavities. Despite the non-retentive cavity shape in some cases, the restoration stayed intact until extraction time, this is due to the good penetration and interlocking with carious dentine. Although X-rays showed good adaptation to cavity walls, there was a gap at the gingival wall in the proximal box. This gap might lead to greater food and bacteria accumulation in a difficult to clean location resulting in continued progress of the disease.

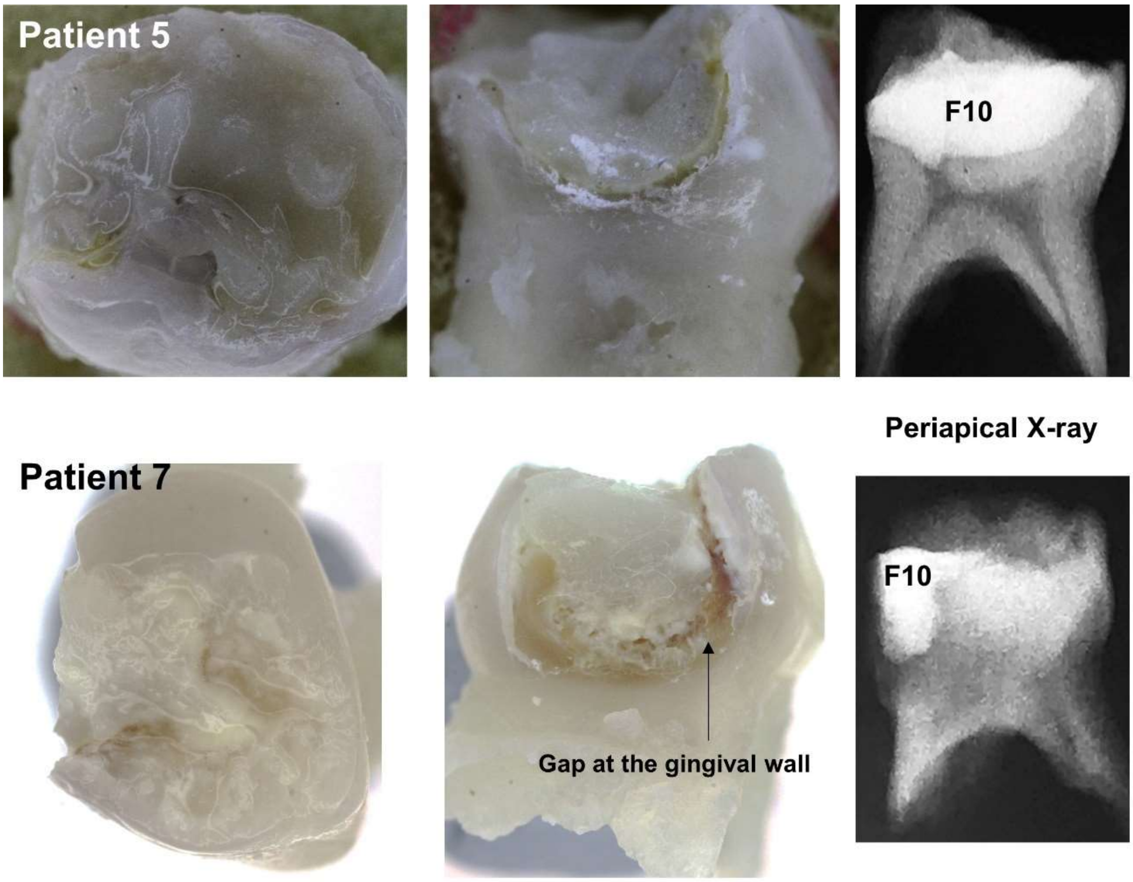

Figure 1 Representative light microscopy images of occlusal and proximal surfaces and X-ray images of patients 5 (top row) and patient 7 (lower row). There is good adaptation except at the gingival wall in the proximal box which suggests difficulty in placing or limited accessibility.

Therefore, adjusting the placement method may be required, maybe by using a floss, a sectional matrix system or celluloid strips for permanent restorations. None of which is time consuming, complex or likely to cause distress to the patient. Squeezing the composite paste starting from the deepest area on the gingival wall while pulling the nozzle upwards could also be beneficial. These techniques were neither optimised nor employed in the trial as the primary objective was assessment of safety. Furthermore, the filling was expected to be a temporary solution only so taking greater time to optimise placement with potential increased patient anxiety was not justified.

CLSM scans (Figure 2) also showed the ability of SMART composite to penetrate into carious dentine, confirming the results previously obtained in the lab. When collagen structure was totally destroyed the composite penetrated into gaps but not dentinal tubules (patient 2).

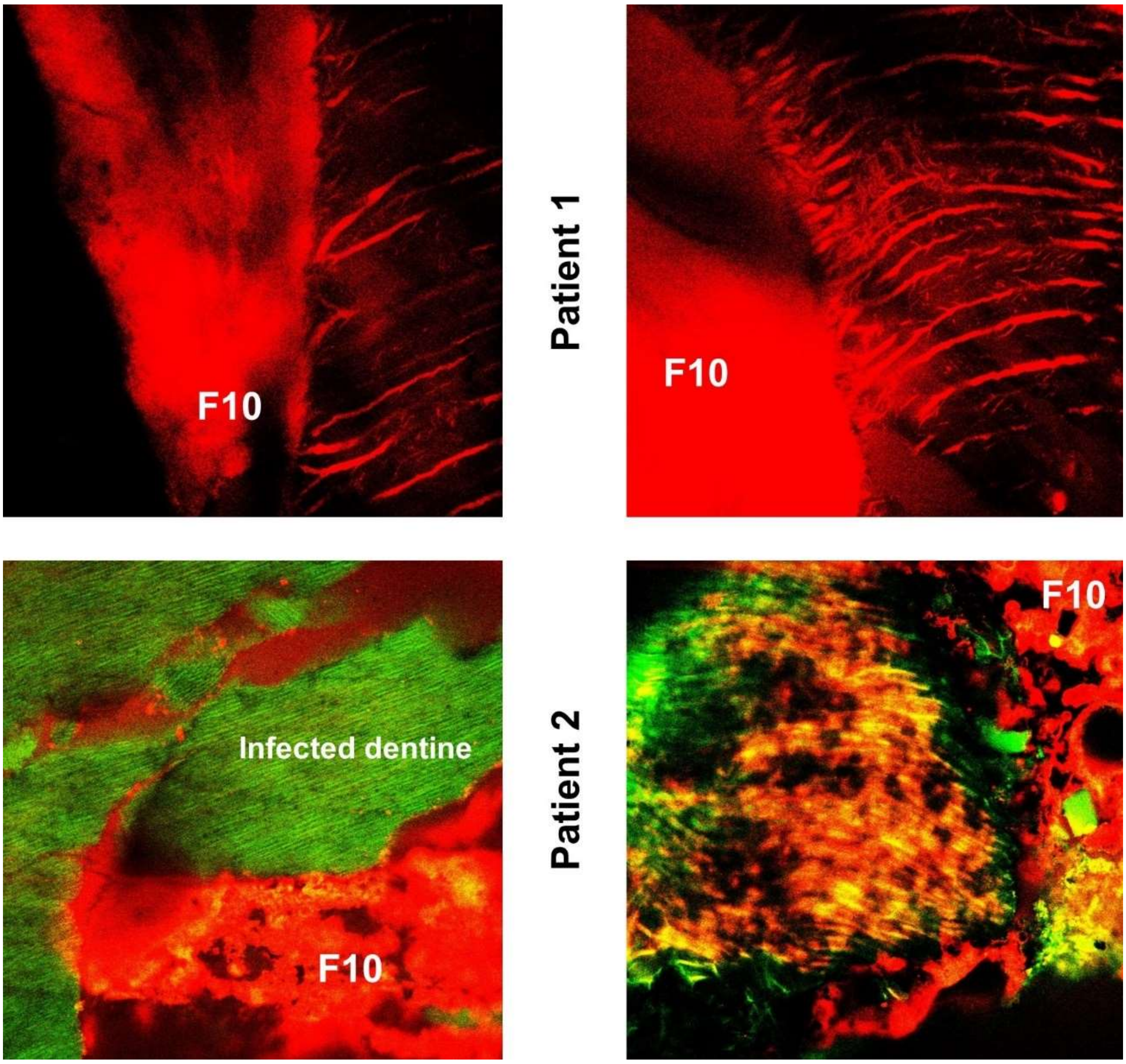

Figure 2 CLSM images of the adhesion interface in teeth extracted from patient 1 (top row) and patient 2 (bottom row). SMART composite (F10) formed resin tags when the collagen structure was less destructed (patient 1) but could also interlock with and thereby stabilise more carious and compacted dentine (patient 2)

SMART composite was optimised to be used in smaller cavities than in the trial where caries has not reached the pulp. Selecting grossly carious teeth for this trial was justified, however, by the need to recruit teeth that were indicated for extraction. This has ensured risk reduction but also enabled laboratory investigations providing confirmation of the highly effective sealing and bonding capability of SMART composite.

- **Conclusions**

SMART composite :

- Gave no adverse effects when placed in teeth of 7 patients
- Could be placed using an minimal restorative technique even with grossly carious cavities
- Remained stable in the cavity even in cases where the tooth was under filled
- Was able to penetrate into carious dentine and form extensive resin tags under difficult and challenging clinical conditions.
- Placement requires greater optimisation to avoid gaps at the gingival wall in Class II cavities.

Whilst the patient number was small, the present clinical trial has clearly demonstrated the significant potential of the SMART composite to successfully restore even heavily broken down children's teeth. This has been without the need for extensive drilling and multiple other composite placement steps that currently make composite placement virtually impossible and rarely employed within UK general dental practice for young children. This innovation would address the increasing problems and escalating patient numbers being faced by hospital paediatric dentistry departments following the ban on mercury amalgam in July 2018. It would simultaneously, reduce the need for extraction of children's teeth under general anaesthesia with all the short and long term risks and clinical and emotional complications that this procedure entails.

Appendix A – Images of all extracted teeth

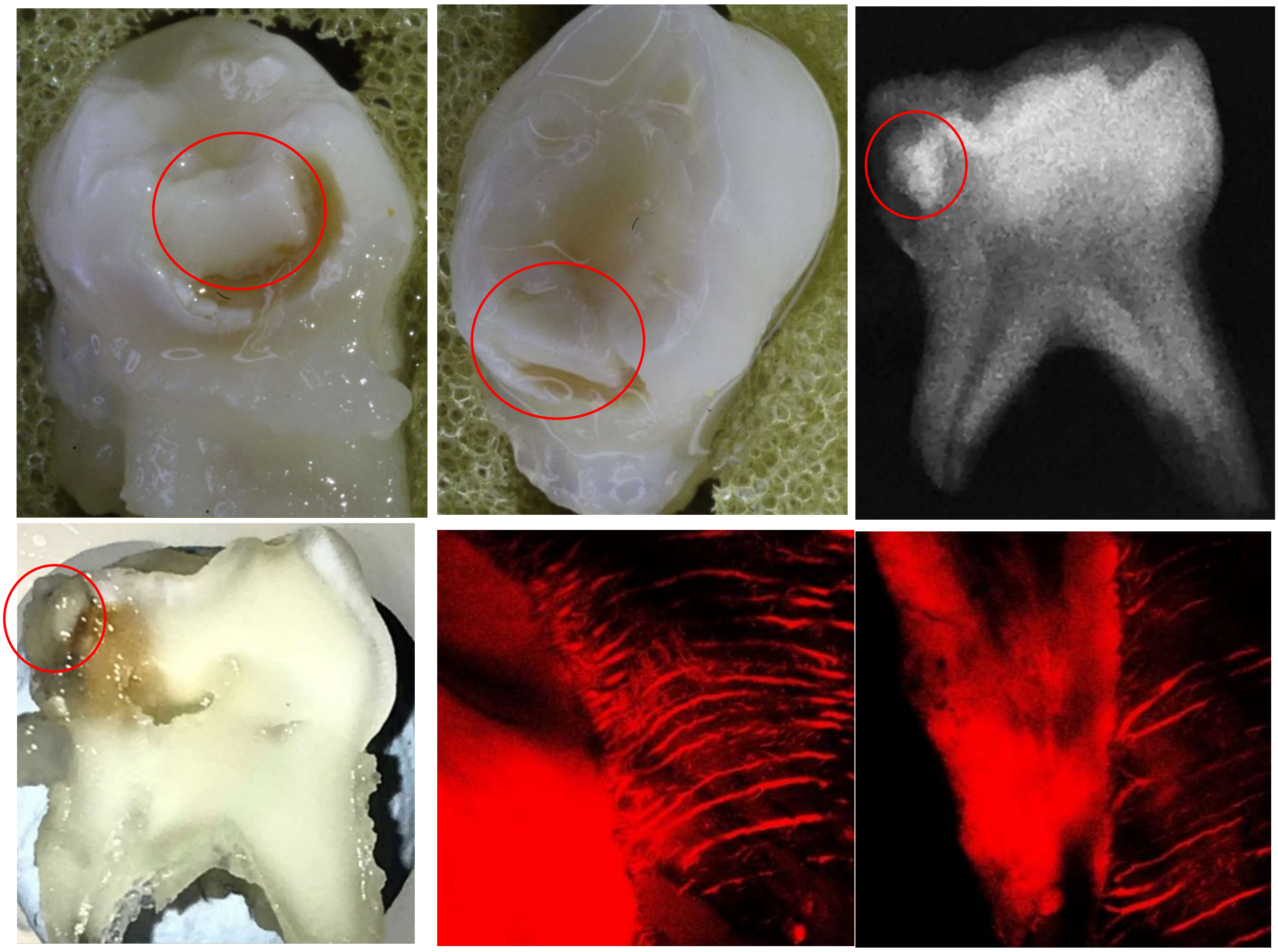

Figure 1A Patient 1 Top left to right - Light microscopy of distal and occlusal restored surfaces and X-ray image. Red circles indicate filling material.

Bottom left to right- Optical image of sectioned tooth and CLMS images showing red Rhodamine B fluorescence in the composite. Images are near the top and at the lower tip of the restoration and 204 micron by 204 micron square. The restoration is ~1mm thick and 2mm deep. The brown dentine colour confirms caries has penetrated to the pulp. The long red (resin) tags in the CLMS images shows the composite material has penetrated deep into, and is interlocked with, the dentine tubules. This explains how the material remained in place even during tooth extraction and sectioning. These tags seal the tubules in the tooth structure and thereby slow the continuing decay process whilst the surface composite restores the tooth surface mechanical properties.

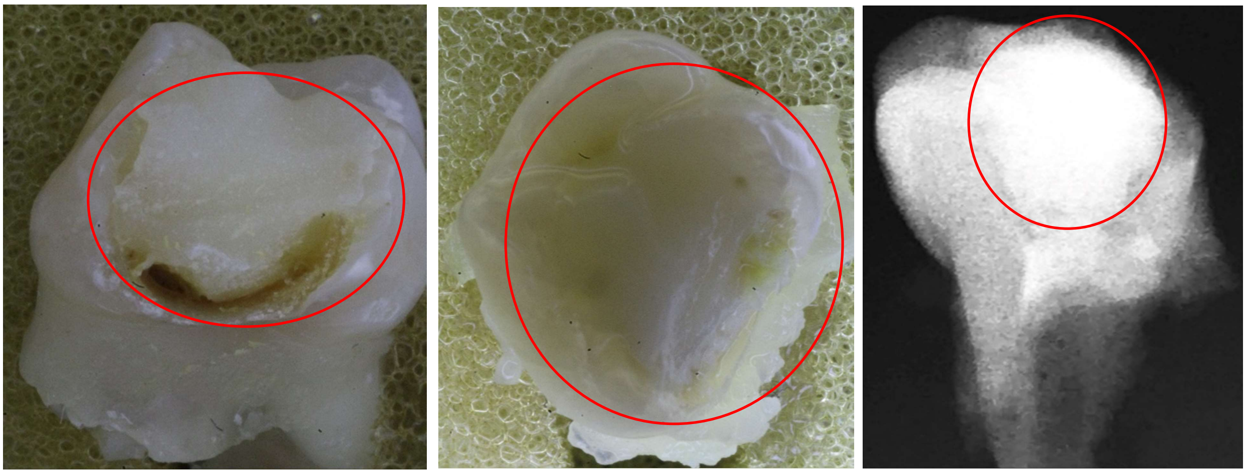

Figure 2A Patient 2 Left to right - Light microscopy of mesial and occlusal surfaces showing SMART composite (highlighted by red rings) and X-ray images. A gap is visible at the gingival margin but material has remained in place even during extraction.

Figure 3A Patient 3 – from left to right - light microscopy of occlusal and distal surfaces and X-ray image with red rings indicating the composite. From the Xray, the composite placement is deeper in the centre of the tooth than on the distal surface.

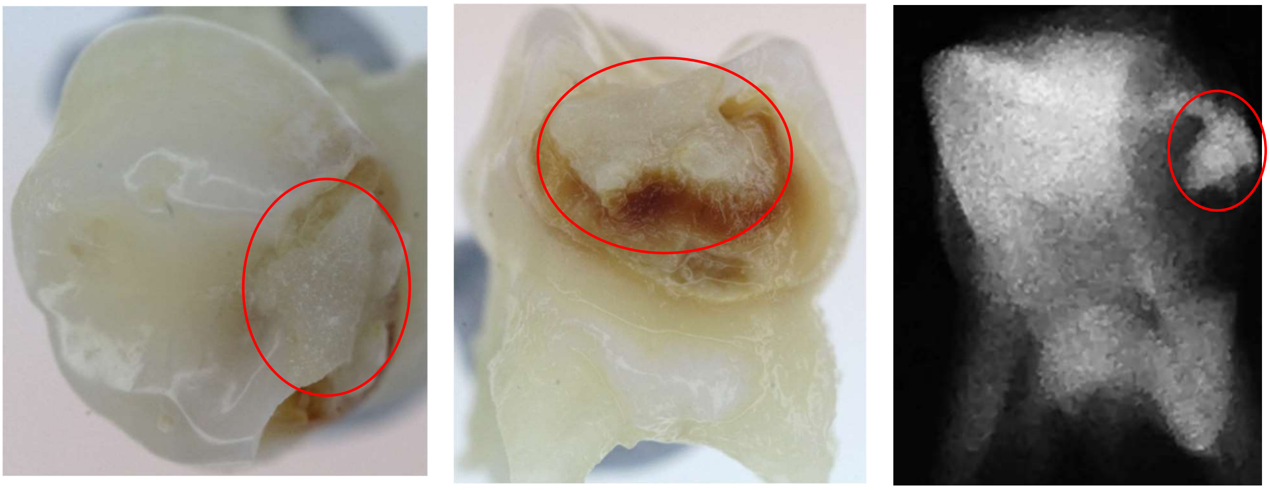

Figure 4A Patient 4. From left to right - Light microscopy of distal and occlusal surfaces of extracted tooth and X-ray image. Red rings indicate the restoration. The none abrupt interface of the composite next to the carious dentine suggests it has penetrated some way into this structure and may thereby have helped to stabilise the carious dentine. From the occlusal surface, bonding of the composite to the enamel looks effective on one side but damaged on the other.

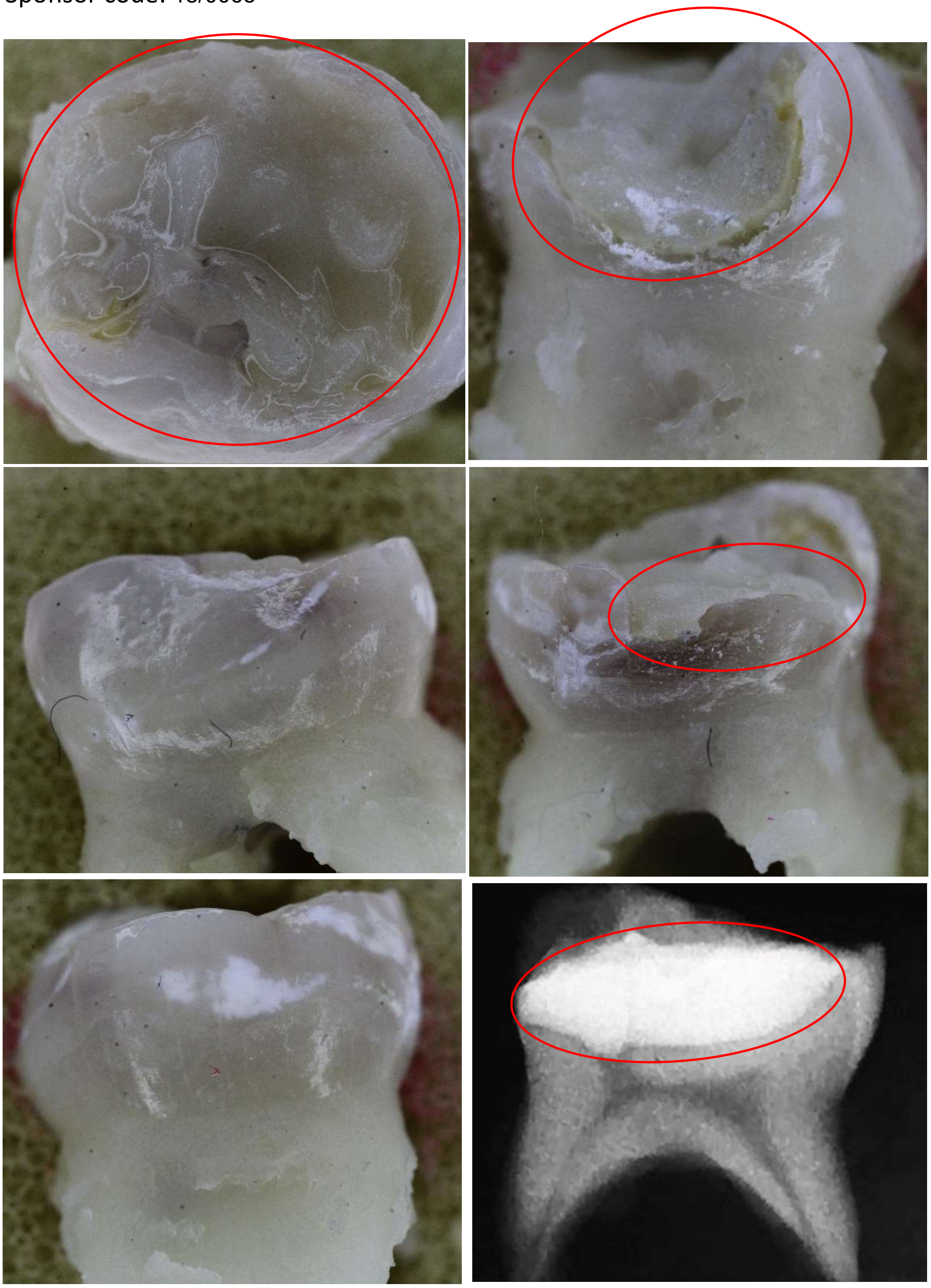

Figure 5A –Patient 5. From left to right then top to bottom - Light microscopy of occlusal, mesial, buccal, lingual and distal surfaces and X-ray of tooth. There is good enamel restoration contact on the occlusal and lingual surfaces but not with the gingival margin on the mesial surface. Careful inspection suggests the composite may be present under the enamel.

Figure 6A Patient 7 From left to right - light microscopy of occlusal and distal surfaces of tooth and X-ray image. From the X-ray the restoration has interlocked well with the highly carious tooth structure. Whilst the restoration on the distal edge is only thin near the gingival margin, upon close examination there appears to be some composite resin covering all the carious dentine.