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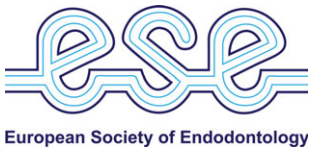
European Society of Endodontology position statement: Revitalization procedures



European Society of Endodontology developed by: K. M. Galler[1], G. Krastl[2], S. Simon[3], G. Van Gorp[4], N. Meschi[4], B. Vahedi[5] & P. Lambrechts[4]

[1]Department of Conservative Dentistry and Periodontology, University Hospital, Regensburg; [2]Department of Conservative Dentistry and Periodontology, University of Würzburg, Würzburg, Germany; [3]Department of Oral Biology and Endodontics, University of Paris Diderot (Paris 7), Paris, France; [4]Department of Oral Health Sciences, KU Leuven and Dentistry, University Hospitals Leuven, Leuven, Belgium; and [5]Private Practice, Augsburg, Germany

Abstract

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This position statement represents a consensus of an expert committee convened by the European Society of Endodontology (ESE) on revitalization procedures. The statement is based on current clinical and scientific evidence as well as the expertise of the committee. The goal is to provide suitably trained dentists with a protocol including procedural details for the treatment of immature teeth with pulp necrosis as well as a patient consent form. Revitalization is a biologically based treatment as an alternative to apexification in properly selected cases. Previously published review articles provide more detailed background information and the basis for this position statement (*Journal of Endodontics*, **39**, 2013, S30; *Journal of Endodontics*, **39**, 2013, 319; *Journal of Endodontics*, **40**, 2014, 1045; *Dental Traumatology*, **31**, 2015, 267; *International Endodontic Journal*, 2015, doi: 10.1111/iej.12606). As controlled clinical trials are lacking and new evidence is still emerging, this position statement will be updated at appropriate intervals. This might lead to changes to the protocol provided here.

Keywords: Endodontology, position statement, regeneration, revitalization.

Introduction

Pulp necrosis in immature teeth due to caries, dental trauma or developmental aberrations poses severe challenges to the dental practitioner. Short roots, thin, fracture-prone dentine walls and wide root canals and apices do not present ideal conditions for conventional root canal treatment. The classic apexification procedure established more than 40 years ago consists of long-term intracanal medication with calcium hydroxide to stimulate the formation of a calcified barrier at the apical foramen. Due to the weakening effect of calcium hydroxide on the thin dentine walls and the resulting high incidence of root fracture (Andreasen *et al.* 2006), this procedure is not advocated any more. Current treatment protocols recommend the placement of an MTA plug to close the apical foramen followed by filling of the root canal with gutta-percha (Simon *et al.* 2007, Parirokh & Torabinejad 2010, Bakland & Andreasen 2012). Although MTA induces a mineralized barrier apically, further root formation cannot be expected, and susceptibility to root fractures due to thin canal walls and poor root-crown ratio remains. However, clinical evidence regarding long-term success and tooth

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Correspondence: Paul M. H. Dummer, Secretary of the European Society of Endodontology, European Society of Endodontology, Postboks 1237 Vika, 0110 Oslo, Norway (e-mail: secretary@e-s-e.eu).

survival is missing, in contrast to calcium hydroxide apexification (Cvek 1992, Andreasen & Bakland 2012). Adhesive materials may be used for intraradicular reinforcement; but again, long-term clinical evidence is missing. Revitalization procedures in immature teeth after pulp necrosis have become part of the endodontic treatment spectrum and should be considered as an alternative to apexification.

This biologically based approach, which is synonymously referred to as 'revascularization' or 'regenerative endodontic procedures' in the literature (for further information see Galler 2015), aims at the (re)generation of pulp-like tissue inside the root canal after inducing an influx of stem cells from the apical papilla. It results not only in a resolution of pain and inflammation, but also in healing of periapical lesions (for review: Hargreaves *et al.* 2013). Furthermore, revitalization can induce an increase of root length and thickness (maturogenesis), which is expected to improve the strength of the root (Hargreaves *et al.* 2013, Wigler *et al.* 2013). The key points of revitalization procedures include the following: (i) minimal or no instrumentation of the dentinal walls, (ii) disinfection with irrigants, (iii) application of an intracanal medicament, (iv) provocation of bleeding into the canal and creation of a blood clot, (v) capping with a hydraulic silicate cement, and (vi) an effective coronal seal. Whether apexification or revitalization generates more favourable clinical outcomes remains controversial (Alobaid *et al.* 2014), although evidence in support of the latter approach is accumulating (Jeeruphan *et al.* 2012). However, histologic analyses after revitalization show that in some cases healing or repair might take place but not regeneration. Repair is defined as ectopic tissue formation with a partial loss of function with studies reporting the formation of fibrous tissue, cementum or bone inside the root canal (da Silva *et al.* 2010, Wang *et al.* 2010, Andreasen & Bakland 2012, Martin *et al.* 2014, Meschi *et al.* 2015).

Regeneration, which is expected to take place after a revitalization procedure, refers to the restoration of the original tissue architecture and function. Pulp-like tissue formation within the root canal is noted where cells differentiate into odontoblasts capable of secreting tubular dentine. From a patient-based perspective, whether it is truly pulp or not may be irrelevant as long as the length and thickness of the root are increased by mineralized tissue apposition and the health of the alveolar bone is maintained.

Case selection and informed consent

Revitalization procedures should be considered in teeth with incomplete root formation with pulp necrosis, whether or not periradicular lesions are present; the aim of treatment being the regeneration of the dentine–pulp complex. Cases that should be excluded from revitalization treatment include avulsed teeth immediately after replantation (as revitalization may occur naturally), impossibility of adequate tooth isolation, and teeth with extensive loss of coronal tissue that require restoration with a post that will occupy the space required for blood clot formation. Recommendations regarding revitalization procedures in cases with luxation injuries cannot be given, as clinical evidence is lacking. For medically compromised patients (ASA physical status classification system ASA III and higher), it may be more prudent to rely on conventional treatments.

The patient, parents or legal guardian must be provided with both general and specific information regarding the:

- existing pathosis;
- regenerative procedure with its potential advantages and current uncertainties compared to conventional therapies;
- time course of treatment and follow-ups;
- use of materials and medicaments as well as the treatment alternatives; and
- likely outcomes.

As the procedure is relatively new, data on long-term survival and tooth stability are missing. A first short-term outcome study documents a higher survival rate after revitalization compared to MTA or calcium hydroxide apexification (Jeeruphan *et al.* 2012); however, the study is limited by a relatively small number of cases per group.

A patient consent form including the points discussed above is available (see Appendix 1).

Protocol including procedural details

First appointment

- Perform clinical diagnostics according to the checklist (see Appendix 2);
- Tooth cleaning, local anaesthesia (optional), field isolation and disinfection (with, e.g. iso-Betadine);
- Prepare access cavity;
- Remove loose or necrotic pulp tissue using suitable endodontic instruments;

- Avoid mechanical instrumentation of the root canal walls;
- Irrigate with 1.5–3% sodium hypochlorite (20 mL, 5 min), use of side-vented needle, place 2 mm above vital tissue (which can be controlled using an operating microscope or when the patient reports pain). The choice of sodium hypochlorite concentration reflects the need for a balance between sufficient disinfection and tissue preservation (Martin *et al.* 2014);
- Bleeding or exudate (control with paper points) may require extended irrigation;
- Irrigate with sterile physiological saline (5 mL) to minimize the cytotoxic effects of sodium hypochlorite on vital tissues;
- Dry with paper points;
- Irrigate with 20 mL of 17% EDTA;
- Insert a nondiscolouring calcium hydroxide product (Lenherr *et al.* 2012) homogenously into the root canal. For most published case reports, antibiotics, mainly triple antibiotic paste consisting of ciprofloxacin, metronidazole and minocycline (Hoshino *et al.* 1996) were used with good results. Drawbacks such as discolouration (Lenherr *et al.* 2012), cytotoxicity (Ruparel *et al.* 2012), sensitization, development of resistance and difficulty of removal from the root canal (Berkhoff *et al.* 2014) need to be taken into account. Recent publications advocate the use of calcium hydroxide (for reviews see Bezgin & Sönmez 2015, Galler 2015, Kontakiotis *et al.* 2014);
- Place coronal seal directly onto intracanal dressing with a minimum thickness according to the material selected.

Second appointment (2–4 weeks later)

- Clinical diagnostics according to the checklist (see Appendix 2);
- If signs of inflammation have not subsided, refresh calcium hydroxide. Administration of systemic antibiotics may be considered if the patient reports general health alteration such as fever or dysphagia (for further information see recommendations of the European Academy of Paediatric Dentistry/EAPD);
- Cleaning, anaesthesia, field isolation and disinfection of operating field. The chosen anaesthesia should feature optimal bone penetration. Current recommendations specify the use of anaesthetics without vasoconstrictor; however, the creation of a blood clot is mostly hampered by the patients' sensation of pain, and evidence describing improved bleeding without vasoconstrictor is sparse (Petrino *et al.* 2010). Experiences from the first visit regarding patient compliance, anxiety and pain control should be taken into account;
- Remove temporary seal;
- Irrigate with 17% EDTA (20 mL, 5 min), use of side-vented needle and place 2 mm above vital tissue;
- Irrigate with sterile physiological saline (5 mL) to reduce adverse effects of irrigants on target cells;
- Remove excess liquid with paper points;
- Induce bleeding by mechanical irritation of periapical tissue and rotational movement of an apically pre-bent file (e.g. size 40 Hedström);
- Allow the canal to fill with blood until 2 mm below the gingival margin to wait for blood clot formation for 15 min;
- Cut a collagen matrix (e.g. Parasorb Cone (Resorba, Medical GmbH, Germany), Collaplug (Integra LifeSciences Corp., Plainsboro, NJ, USA) or Hemocollagene (Septodont, Saint Maur des Fossés, France) to a diameter larger than the coronal part of the root canal and a height of 2–3 mm, place on top of the blood clot, allow the matrix to soak with liquid to avoid formation of a hollow space;
- Place a hydraulic silicate cement (e.g. MTA or tricalcium silicate cement) on top of the collagen matrix in a thin homogeneous layer of about 2 mm underneath the cement–enamel junction and beware of potential discolouration after contact of the material with blood;
- Apply a flowable, light-curable glass–ionomer or calcium hydroxide cement;
- Refresh the cavity walls with a diamond bur or grit blast with aluminium oxide;
- Seal with adhesive restoration.

Follow-up

Follow-ups should be performed after 6, 12 and 18 and 24 months, after that annually for 5 years. A 3-month follow-up is recommended in cases of long-standing infection, difficult elimination of signs of inflammation (e.g. second application of intracanal dressing), the presence of inflammatory root resorption or where alternative treatment (e.g. autotransplantation) has to be considered. Clinical and

radiographic diagnostics should be performed according to the flow chart.

In the case of planned orthodontic treatment, it should be recognized that teeth after revitalization may be more perceptible to inflammation and apical root resorption (Kindelan *et al.* 2008). Thus, bony healing should be awaited, and teeth after revitalization should be excluded from orthodontic treatment or follow-up intervals should be shortened during orthodontic treatment.

Success criteria

- No pain;
- No signs and symptoms of inflammation;
- Healing of pre-existing bony periapical lesion;
- Increase of root thickness and length;
- Absence of (continued) external root resorption;
- Positive response to sensibility testing;
- Patient acceptance;
- No unacceptable colour changes;
- Radiographic detection of a new PDL along the inner wall of the root canal.

Assessment and future perspective

Regenerative endodontic procedures have become part of the endodontic treatment spectrum. Clinicians with suitable training should be aware of the procedure and consider it as an alternative treatment to apexification based on the individual case. A growing body of evidence that shows the clinical feasibility of this approach makes it likely that regenerative endodontic therapies will become established procedures in endodontic practice.

Conflict of interest

The authors have stated explicitly that there is no conflict of interest in connection with this article.

References

Alobaid AS, Cortes LM, Lo J *et al.* (2014) Radiographic and clinical outcomes of the treatment of immature permanent teeth by revascularization or apexification: a pilot retrospective cohort study. *Journal of Endodontics* **40**, 1063–70.

Andreasen JO, Bakland LK (2012) Pulp regeneration after non-infected and infected necrosis, what type of tissue do we want? A review. *Dental Traumatology* **28**, 13–8.

Andreasen JO, Munksgaard EC, Bakland LK (2006) Comparison of fracture resistance in root canals of immature sheep teeth after filling with calcium hydroxide or MTA. *Dental Traumatology* **22**, 154–6.

Bakland LK, Andreasen JO (2012) Will mineral trioxide aggregate replace calcium hydroxide in treating pulpal and periodontal healing complications subsequent to dental trauma? A review. *Dental Traumatology* **28**, 25–32.

Berkhoff JA, Chen PB, Teixeira FB, Diogenes A (2014) Evaluation of triple antibiotic paste removal by different irrigation procedures. *Journal of Endodontics* **40**, 1172–7.

Bezgin T, Sönmez H (2015) Review of current concepts of revascularization/revitalization. *Dental Traumatology* **31**, 267–73.

Cvek M (1992) Prognosis of luxated non-vital maxillary incisors treated with calcium hydroxide and filled with gutta-percha. A retrospective clinical study. *Endodontics & Dental Traumatology* **8**, 45–55.

Galler KM (2015) Clinical procedure for revitalization: current knowledge and considerations. *International Endodontic Journal* doi: 10.1111/iej.12606 [Epub ahead of print].

Hargreaves KM, Diogenes A, Teixeira FB (2013) Treatment options: biological basis of regenerative endodontic procedures. *Journal of Endodontics* **39**, S30–43.

Hoshino E, Kurihara-Ando N, Sato I *et al.* (1996) *In-vitro* antibacterial susceptibility of bacteria taken from infected root dentine to a mixture of ciprofloxacin, metronidazole and minocycline. *International Endodontic Journal* **29**, 125–30.

Jeeruphan T, Jantarat J, Yanpiset K, Suwannapan L, Khewsawai P, Hargreaves KM (2012) Mahidol study 1: comparison of radiographic and survival outcomes of immature teeth treated with either regenerative endodontic or apexification methods: a retrospective study. *Journal of Endodontics* **38**, 1330–6.

Kindelan SA, Day PF, Kindelan JD, Spencer JR, Duggal MS (2008) Dental trauma: an overview of its influence on the management of orthodontic treatment. Part 1. *Journal of Orthodontics* **35**, 68–78.

Kontakiotis EG, Filippatos CG, Agrafioti A (2014) Levels of evidence for the outcome of regenerative endodontic therapy. *Journal of Endodontics* **40**, 1045–53.

Lenherr P, Allgayer N, Weiger R, Filippi A, Attin T, Krastl G (2012) Tooth discoloration induced by endodontic materials: a laboratory study. *International Endodontic Journal* **45**, 942–9.

Martin DE, De Almeida JF, Henry MA *et al.* (2014) Concentration-dependent effect of sodium hypochlorite on stem cells of apical papilla survival and differentiation. *Journal of Endodontics* **40**, 51–5.

Meschi N, Hilkens P, Lambrichts I *et al.* (2015) Regenerative endodontic procedure of an infected immature permanent human tooth: an immunohistological study. *Clinical Oral Investigations* [Epub ahead of print].

Parirokh M, Torabinejad M (2010) Mineral trioxide aggregate: a comprehensive literature review–Part III: Clinical applications, drawbacks, and mechanism of action. *Journal of Endodontics* **36**, 400–13.

Petrino JA, Boda KK, Shambarger S, Bowles WR, McClanahan SB (2010) Challenges in regenerative endodontics: a case series. *Journal of Endodontics* **36**, 536–41.

Ruparel NB, Teixeira FB, Ferraz CC, Diogenes A (2012) Direct effect of intracanal medicaments on survival of stem cells of the apical papilla. *Journal of Endodontics* **38**, 1372–5.

da Silva LA, Nelson-Filho P, da Silva RA *et al.* (2010) Revascularization and periapical repair after endodontic treatment using apical negative pressure irrigation versus conventional irrigation plus triantibioticintracanal dressing in dogs' teeth with apical periodontitis. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* **109**, 779–87.

Simon S, Rilliard F, Berdal A, Machtou P (2007) The use of mineral trioxide aggregate in one-visit apexification treatment: a prospective study. *International Endodontic Journal* **40**, 186–97.

Wang X, Thibodeau B, Trope M, Lin LM, Huang GT (2010) Histologic characterization of regenerated tissues in canal space after the revitalization/revascularization procedure of immature dog teeth with apical periodontitis. *Journal of Endodontics* **36**, 56–63.

Wigler R, Kaufman AY, Lin S, Steinbock N, Hazan-Molina H, Torneck CD (2013) Revascularization: a treatment for permanent teeth with necrotic pulp and incomplete root development. *Journal of Endodontics* **39**, 319–26.

Appendix 1: Patient Consent Form

Revitalization

Dear parent or legal guardian,

The dental examination of your child has shown that due to unusual anatomy, dental decay or trauma, the loss of the inner soft tissue (dental pulp or 'nerve') has occurred in a tooth with incomplete root formation. This document provides information regarding a biology-based treatment as an alternative to conventional treatment, which opens the possibility of a better prognosis.

General information

At the time of tooth eruption, the formation of the root below the gum that anchors the tooth in its bony socket is not complete. In fact, it takes 2–3 years for the root to become fully developed. If damage to the dental pulp occurs before the root is fully developed, the dentist faces a number of problems:

- The loss of the dental pulp (nerve) stops any further root development;
- Immature teeth have a wide root canal, thin canal walls that are prone to fracture and a wide open apex at the root tip. These conditions do not allow for conventional root canal treatment;
- Following infection in the pulp subsequent problems may include inflammation of the surrounding bone, resorption of tooth root or surrounding bone, increased tooth mobility and eventually tooth loss.

Conventional therapy and treatment options

Apexification

Conventional treatment involves thorough disinfection of the root canal and insertion of a biocompatible and bioactive cement as an apical barrier towards the tip of the root. The material induces the formation of hard tissue at the root tip. The disadvantage of apexification is that the pulp does not regain vitality and that the root length and thickness do not increase; in other words, the tooth remains weak.

No treatment

Bacteria inside the root canal can spread to the surrounding bone and cause inflammation, which can lead to abscess formation and premature tooth loss.

Extraction

Extraction of the tooth requires replacement, either by an implant or a prosthodontic bridge, autotransplantation or orthodontic space closure. Implants and bridges should be performed only in adult patients after skeletal growth is complete (20–30 years of age).

Extraction and autotransplantation

After extraction of a damaged incisor, it can be replaced with a posterior tooth, for example a premolar, if root development of this posterior tooth is at the correct stage. This procedure requires extraction and transplantation of the posterior tooth in the position of the incisor.

Biology-based treatment – revitalization

The treatment we are planning requires at least two visits. During the first visit, access to the pulp chamber and root canal is achieved and the pulp tissue remnants are removed. The access cavity is placed on the palatal or lingual aspect of the tooth and is not visible from the outside. The tooth will be shielded (normally with a rubber dam) to avoid contamination with saliva. The root canal inside the tooth will be disinfected with irrigant solutions, and a medicament is placed into the canal before placement of a temporary filling. The medicament is usually calcium hydroxide; however, if signs of inflammation persist, the use of an antibiotic mix inside the root canal may be indicated. With the exception of the antibiotic mix, all these stages are part of regular endodontic treatment.

On the second visit, the temporary filling and medicament are removed. After repeated rinsing with antiseptics, bleeding is induced into the canal by mechanical irritation of the tissue at the root tip with a hand instrument. After 10–15 min, a blood clot will form inside the root canal, which is then covered with a collagen sponge, a layer of bioactive cement and the permanent filling. All measures are normally performed under local anaesthesia and are free of pain. An exception might be the use of the hand file to induce bleeding, which can cause mild irritation but is not painful.

Advantages

The goal of the treatment is to repopulate the root canal with vital living tissue in order for root development to continue. This leaves the tooth with thicker and stronger root walls and allows the bony lesion to heal. Regeneration of the dental pulp can be induced by stem cells, which reside in the apical part of the root of immature teeth. With the induction of bleeding, they can flow into the root canal and induce complete root formation.

If the described treatment does not lead to a successful outcome, conventional treatment can still be attempted.

Assessment and risks

Revitalization is a fairly new treatment option that has been described in the dental literature in case reports and case series in the past 10 years. However, there are only a small number of clinical trials, and an agreed clinical technique has not been developed. The procedure is promising, but treatment success depends on several factors, including type and duration of the inflammation as well as an individual's healing and defence mechanisms.

After treatment, pain can occur in some cases. If it does not subside, please return to the clinic to consider other treatment options.

The treatment may lead to discolouration of the crown, which might be aesthetically unfavourable.

Follow-up

After initial treatment, follow-up visits are necessary to observe the healing process. This includes regular clinical and radiographic examinations, initially after 3, 6, 9, 12 and 18 months, after that every year for the next 5 years.

Patient consent

I confirm that I have been informed comprehensively regarding the planned treatment. All my questions have been answered.

Date, Place Signature

Appendix 2: Revitalization: Pre-operative Diagnostics

Patient					
Age					
Gender					
Affected tooth					
Chief complaint					
Medical and dental history					
Drugs used before treatment					

	Yes	No	Remarks		
Clinical Examination					
Response to cold thermal pulp test					
Response to electric pulp test					
Tenderness to percussion					
Tooth mobility					
Ankylotic percussion tone					
Pain on palpation					
Swelling					
Sinus tract					
Coronal discolouration					
Probing depth	»		mb:	b:	db:
			ml:	l:	dl
Cracks					
Radiographic Analysis					
Periapical lesion			Size:		
Apical foramen	»		Size:		
CBCT analysis					