Apically Extruded Sealers: Fate and Influence on Treatment Outcome

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Abstract

Introduction: This retrospective study evaluated cases of unintentional overfillings for the fate of the extruded sealers and their influence on treatment outcome. **Methods:** One hundred five teeth treated by a single operator and exhibiting overfillings in the postobturation radiograph were included in the study. Seventy-five teeth exhibited apical periodontitis lesions at the time of treatment. Sealers included Pulp Canal Sealer (Sybron Dental, Orange, CA), PCS Extended Working Time-EWT (Sybron Dental), Tubli-Seal (Sybron Endo), Endomethasone (Septodont, Saint-Maur-des-Fossés, France), AH Plus (DeTrey GmbH, Konstanz, Germany), and Apexit (Ivoclar Vivadent, Schaan, Lichtenstein). Recall radiographs were compared with immediate postobturation films for removal of the extruded material and status of the periradicular tissues. Data were grouped as 1-, 2- and >4-year recall and statistically analyzed using the chi-square and Fisher exact tests. **Results:** As for the sealers' fate, the only statistically significant differences at the 1-year recall were observed when comparing Tubli-Seal with AH Plus, Apexit, and Endomethasone ($P < .05$). At both the 2- and 4-year recalls, frequency of complete removal of AH Plus and Apexit was significantly lower when compared with all the other sealers ($P < .05$). No other significant differences were observed between groups. As for the influence on treatment outcome, there were no statistically significant differences between sealers at all follow-up periods ($P > .05$). Data from the >4-year recall revealed that 79% of the teeth with apical periodontitis lesions at the time of treatment had healed in comparison with 100% of the teeth with no apical periodontitis ($P < .01$). **Conclusions:** Not all extruded sealers were predictably removed from the periradicular tissues. Treatment outcome was not significantly affected by the type of extruded sealer. A significantly better outcome was observed for teeth with no lesion in comparison with teeth with apical periodontitis. *(J Endod 2016;42:243–249)*

Key Words

Endodontic sealers, endodontic treatment, overfilling, treatment outcome

Root canal obturation serves the main purpose of impeding the traffic of fluids from the periradicular tissues or saliva into the canal as well as bacteria and their virulence factors and antigens from the canal to the periradicular tissues (1). Ideally, the filling material should be restricted to the intraradicular space (2, 3). Studies have shown that the highest success rate of endodontic treatment is observed for teeth with root canal fillings ending 0–2 mm short of the radiographic apex, and cases with underfillings or overfillings display significantly lower rates (3–5).

However, there are circumstances in which it is not possible to control application of the material, and some apical extrusion occurs. In addition, the use of some thermoplasticized gutta-percha filling techniques is also associated with a higher incidence of filling material extrusion (6). When extruded, the fate of the filling material will depend on its solubility in the tissue fluids and susceptibility to phagocytosis, whereas its influence on treatment outcome arguably depends on the material's biocompatibility. It has been suggested that the lower healing rate associated with overfillings is a result of the cytotoxicity of the root filling material (7) or a foreign body reaction to some of its constituents (8, 9). However, evidence indicates that the apical extent of root canal fillings seems to have no direct correlation to treatment failure provided infection is absent (10–12). Overfilling may impair the prognosis of treatment of infected teeth with apical periodontitis, and this is possibly related to a deficient apical seal and/or previous overinstrumentation causing extrusion of infected debris (13). It has also been suggested that the extraradicular occurrence of a filling material may slow down the healing process of apical periodontitis (14).

Information on sealers' fate and influence on the outcome when apically extruded is scarce in the literature. A study evaluated the radiographic appearance of unintentionally extruded filling material and found that 2 zinc oxide and eugenol-based sealers were completely removed over time, and overfillings per se had no influence on treatment outcome (15). Studies have compared the effects of different sealers on the outcome (16–19), but none of them focused specifically on overfilling cases. Therefore, the present study was intended to evaluate cases of unintentional overfillings after using different sealers for the fate of the extruded material and its influence on endodontic treatment outcome.

Materials and Methods

The teeth included in this retrospective study are a fraction of a number of teeth treated by a single operator in his private office using a standardized treatment protocol over a period of 30 years. In general, 1437 root canal–treated teeth (from 830 patients) were available for 1 or multiple follow-ups. Part of this sample ($n = 816$) was the object

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of a previous follow-up study (5). Teeth exhibiting overfillings in the postobturation radiograph (n = 105), with follow-up examinations ranging from 1 year to up to 30 years, were selected for analysis in the present study. Teeth with overextended gutta-percha points were not included. Seventy-five teeth presented with apical periodontitis lesions at the time of treatment as determined radiographically, whereas 30 teeth had normal apical tissues.

Treatment Procedures

A diagnosis of "vital" or "necrotic" pulp was made on the basis of clinical signs and symptoms and periapical radiographs. All endodontic treatments were performed using a strict aseptic technique. After rubber dam isolation and field disinfection with 30% H_2O_2 and 5% tincture of iodine, the working length was established at the apical constriction. This was accomplished by radiography alone and, since the late 1990s, with the help of an electronic apex locator checked with radiographs. Efforts were made to machine an apical "stop" at or near the apical constriction to adjust a gutta-percha master cone of appropriate size. After preflaring the coronal two thirds of the root canal with Gates-Glidden burs and hand instruments (Hedström files), the apical third was instrumented by using hand instruments (Hedström and K-type files). In all cases, care was taken to avoid the instrument passage beyond the working length (ie, patency files were not used). Irrigation was frequently made using copious amounts of 1% sodium hypochlorite with a minimum needle size. Teeth with the diagnosis of necrotic pulp were treated in 2 visits with an interappointment medication with calcium hydroxide, whereas teeth with a diagnosis of vital pulp were treated in a single visit.

The root canals were filled with laterally compacted gutta-percha and a sealer. Different sealers were randomly used and included the zinc oxide and eugenol-materials Pulp Canal Sealer (PCS; Sybron Dental, Orange, CA), PCS Extended Working Time (EWT) (Sybron Dental), Tubli-Seal (Sybron Dental), and Endomethasone (Septodont, Saint-Maur-des-Fossés, France); the resin-based sealer AH Plus (DeTrey GmbH, Konstanz, Germany); and the calcium hydroxide–based sealer Apexit (Ivoclar Vivadent, Schaan, Lichtenstein). After completion of the endodontic treatment, an appropriate restoration was placed (direct restoration in cases with moderate tooth structure loss or indirect restoration when cuspal coverage was indicated).

Follow-up Examination and Data Analyses

At each follow-up occasion, at least 1 periapical radiograph in conventional straight projection was taken. Additional mesial- or distal-angled radiographs were taken in cases with more than 1 root canal in the same root. Radiographic examination was performed using the long cone technique (Explor-X 65 kV; Fiad, Trezzano, Italy, or Irix 70; Trophy, Marne-la-Vallée, France) with Kodak Ultraspeed film 31 × 41 (DF 58) or 22 × 35 (DF 54; Eastman Kodak Company, Rochester, NY). A film holder (Rinn Corp, Elgin, IL) was used in the large majority of cases, except when the patient did not cooperate. Radiographs were processed manually in a darkroom following the recommendation of the manufacturer. In later periods, some digital systems were also used including RVG Gold (Trophy), Kodak RVG 6100 (Carestream Health, Atlanta, GA), and VistaScan Mini Plus (Dürr Dental AG, Bietigheim-Bissingen, Germany). Conventional radiographs were scanned (images were at least 10 × 15 cm at 300 DPI). All radiographs were incorporated in PowerPoint (Microsoft, Redmond, WA) files for further analyses.

Two examiners, who are experienced endodontists and were blinded to the sealer used, individually analyzed and compared the baseline and recall radiographs for the fate of the extruded sealer and treatment outcome. Radiographs were analyzed on the computer screen in a darkened room. For the determination of a sealer's fate, the examiners recorded if the sealer was present or not in the recall radiographs in comparison with the radiographs taken at baseline. For the analysis of treatment outcome, Strindberg's criteria (20) were used. Observers were calibrated against a set of 100 reference teeth. Healthy periradicular conditions were judged when both the contour and width of the periodontal ligament space were normal or the periodontal ligament contour was only slightly widened around excess filling. The appearance of the surrounding bone was normal. Diseased teeth presented any discernible apical radiolucency (20). For the follow-up periods of 1 and 2 years, another category was included (ie, "healing," which was attributed to teeth that still showed lesions but with reduced sizes in comparison with the baseline radiograph). In multirooted teeth, only the roots with overfillings were evaluated and recorded individually. When evaluations of fate and outcome provided by the 2 examiners disagreed (kappa values = 0.86 and 0.76, respectively, for fate and outcome analyses), a third experienced examiner was consulted.

Data Analysis

For statistic analyses comparing the periradicular presence/absence (fate) of the different sealers and their influence on the outcome, data were grouped as 1-, 2- and >4-year recall and analyzed by means of the chi-square test with Yates' correction and the Fisher exact test. The effect of the previous status of the periradicular tissues (healthy or diseased) on the outcome of teeth with overfillings was also compared by means of the Fisher exact test. The significance level was set at 5% ($P < .05$).

Results

Overall, 105 teeth having overfillings at baseline were included in the study. Of these, 63 were available for the 1-year follow-up, 73 for the 2-year follow-up (57 of which were also evaluated at 1 year), and all of them for the >4-year follow-up.

Fate of the Extruded Sealer

At the 1-year follow-up, 3 cases from the Tubli-Seal group were examined, and in all of them the extruded material had completely disappeared. Complete removal was also observed for 6 of 14 (43%) and 5

TABLE 1. The Fate of Different Sealers after Unintentional Extrusion to the Periradicular Tissues over Different Follow-up Periods

		1-year follow-up		2-year follow-up		>4-year follow-up		
Sealer	Baseline *n*	Present	Absent	Present	Absent	Present	Absent	Absent %
AH Plus	20	13	1	16	1	17	3	15
Apexit	15	7	2	8	0	10	5	33
Endomethasone	15	7	2	4	5	2	13	87
PCS	28	8	6	8	8	5	23	82
PCS EWT	21	9	5	9	10	6	15	71
Tubli-Seal	6	0	3	0	4	0	6	100

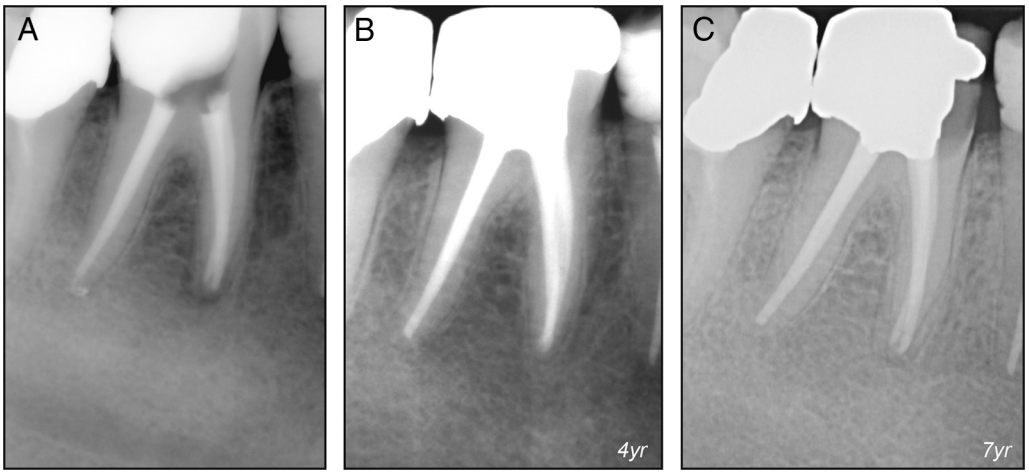

Figure 1. PCS EWT. Tooth 30 with necrotic pulp and apical periodontitis in a 40-year-old woman. (*A*) The postobturation radiograph. Sealer extrusion around the distal root. (*B*) The 4-year follow-up radiograph. The absence of sealer in the periradicular tissues. The case was categorized as healed. Note that the sealer was resorbed also in the most apical canal. (*C*) The 7-year follow-up radiograph. Periradicular conditions are unchanged.

of 14 (36%) of the cases filled with PCS and PCS EWT, respectively (Table 1). However, the only statistically significant differences at this period were observed when comparing Tubli-Seal with AH Plus, Apexit, and Endomethasone ($P < .05$).

At the 2-year recall, the number of cases in which the extruded sealer had disappeared increased for all groups, except for AH Plus and Apexit. The frequency of removal of these 2 sealers was significantly lower when compared with all the other sealers ($P < .05$) (Table 1). No other significant differences were observed between groups ($P > .05$).

At the >4-year evaluation, statistic analysis showed similar findings to the 2-year recall, (ie, significant differences were observed between AH Plus and Apexit when compared with the other sealers [Figs. 1–5]). No other significant differences were observed between groups. Except for Tubli-Seal, no sealer showed 100% disappearance. In most cases of the Endomethasone, PCS, and PCS EWT groups, the extruded material was no longer present. On the other hand, only in a few cases from the AH Plus and Apexit groups was the material completely removed from the periradicular tissues.

Influence on Treatment Outcome

All the 30 teeth with no apical periodontitis lesion at the time of treatment remained without disease at all follow-up intervals regardless of the type of extruded material (Table 2).

At the 1-year recall, 43 teeth with apical periodontitis at the time of treatment were available for evaluation. Of these, 20 (46.5%) teeth were classified as healed and 14 (33%) teeth as healing (lesion reduced in size but still present). At the 2-year period, 52 teeth were examined; 31 (60%) and 12 (23%) were categorized as healed and healing, respectively. Data from the >4-year follow-up revealed that 79% of the cases with apical periodontitis lesions at the time of treatment were categorized as healed in comparison with 100% of the teeth with no apical

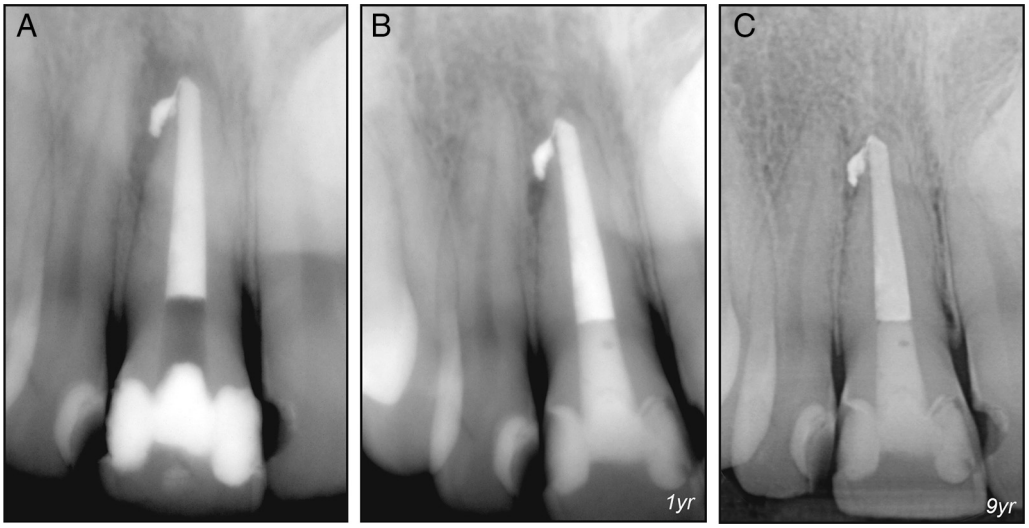

Figure 2. AH Plus. Tooth 8 with necrotic pulp and a buccal sinus tract in a 24-year-old woman. (*A*) The postoperative radiograph. (*B*) The 1-year follow-up; there were no changes in the extruded sealer. (*C*) The 9-year follow-up. The apical periodontitis lesion healed, but the appearance of the extruded sealer remained unchanged.

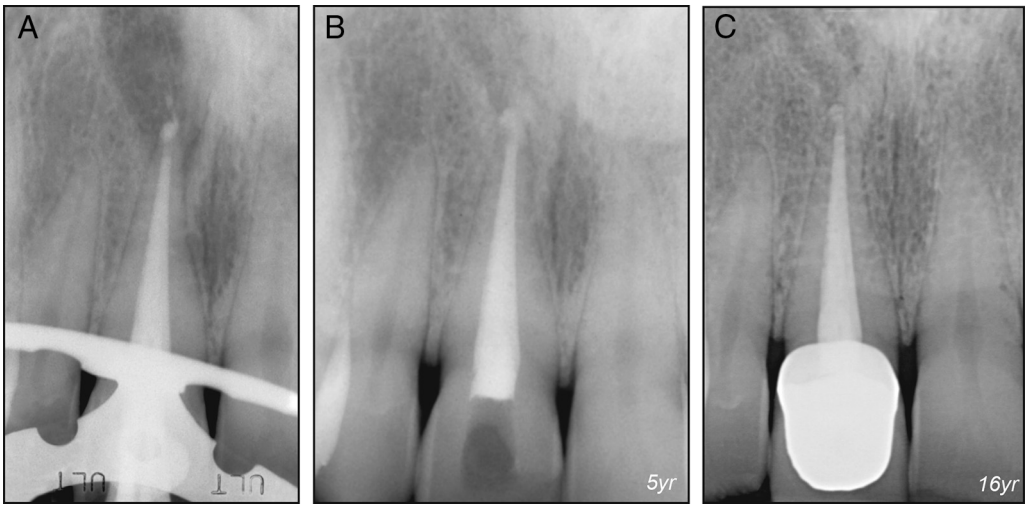

Figure 3. Apexit. Tooth 8 with necrotic pulp and apical periodontitis in a 27-year-old woman. (*A*) The postoperative radiograph. (*B*) The 5-year follow-up. The extruded sealer appears partially removed but is still visible. (*C*) The 16-year follow-up. Normal periradicular conditions can be observed, but some sealer is still discernible in the periradicular tissues. Note that the sealer can still be seen in the most apical canal.

periodontitis. This difference was highly significant ($P < .01$). The incidence of healed rates ranged from 67% for PCS to 91% for PCS EWT (Table 3). There was no statistically significant difference in the outcome between the tested sealers at all examination periods ($P > .05$).

Discussion

This retrospective study evaluated cases of unintentional overfillings during root canal treatment for the fate of the extruded sealer and its influence on the outcome. For the sake of comparison between the materials, follow-up examinations were grouped as 1-year, 2-year, and >4-year periods. Overall, findings revealed that with the passage of time, the zinc oxide eugenol–based sealers had a significantly increased removal rate in comparison with AH Plus, a resinous sealer, and Apexit, a calcium hydroxide–based sealer. As for treatment outcome, there was no significant difference between the different extruded sealers.

When extruded through the apical foramen, sealers may be solubilized in the periradicular tissue fluids, phagocytosed, or encapsulated by fibrous connective tissue (1). The material's fate will depend on its physicochemical properties, especially solubility in water. In this regard, studies have shown a low solubility for AH Plus (21, 22), which can be desirable when taking into account the material's stability in the intraradicular space, but, on the other hand, this may not be the best property when the material is extruded to the periradicular tissues. However, as for Apexit, studies have not shown a significantly lower solubility when compared with other sealers (22, 23). The possibility exists that epoxy resin, the major component of AH Plus, which has also been reported to be present in Apexit (23), may be responsible for the lower removal rates for these sealers.

The present results do not agree with the previous observation from another study (15), which reported that given enough time postoperatively all extruded sealers would be removed. This may be true for the zinc oxide eugenol–based sealers, but only 15% of the AH Plus cases and one third of the Apexit cases showed complete removal of the extruded material in periods longer than 4 years. In the majority of cases in which these sealers were not removed, they remained apparently unchanged on radiographs, even after long periods ranging from 10 years (8 AH Plus cases) to 16 years (3 Apexit cases) (Figs. 2–4).

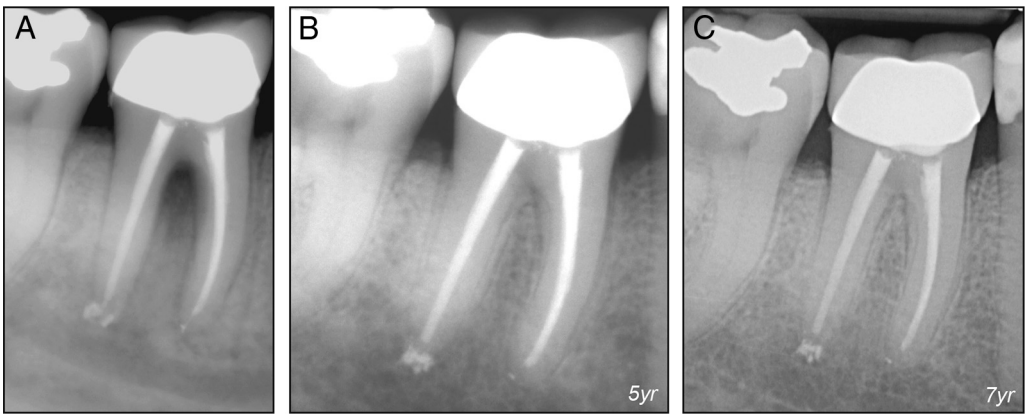

Figure 4. AH Plus. Tooth 30 with necrotic pulp, apical periodontitis, and severe bone loss in the furcation in a 51-year-old woman. (*A*) The postoperative radiograph. Large extrusion of sealer periapically to the distal root; a minor extrusion is also present around the mesial root. (*B*) The 5-year follow-up. The periapical and inter-radicular lesions healed completely, whereas the extruded sealer maintained the same appearance. (*C*) The situation is the same at the 7-year follow-up.

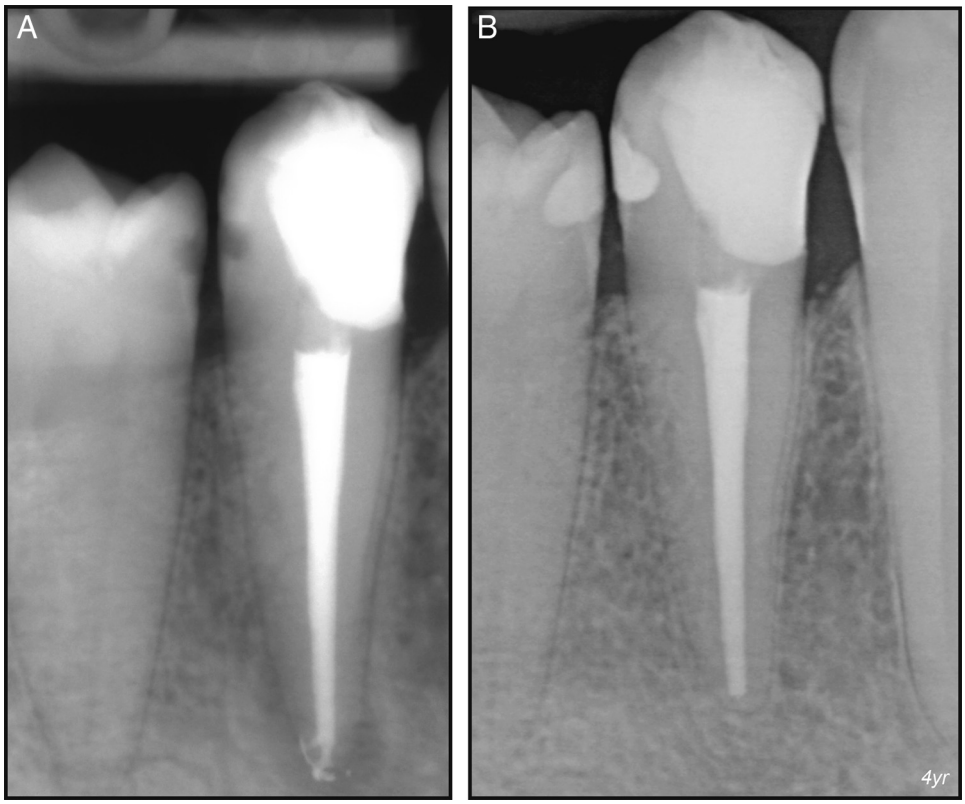

Figure 5. PCS EWT. Tooth 28 with necrotic pulp and apical periodontitis in a 37-year-old man. (*A*) The postoperative radiograph. Sealer was pushed into the periapex through the main foramen, and an apical ramification was present on the distal apical profile. (*B*) The 4-year follow-up. The apical periodontitis lesion healed completely, and the extruded sealer is no longer visible. Note that the sealer can no longer be seen in both the most apical canal and apical ramification.

Despite the differences observed in the removal of the different sealers, none of them was found to influence treatment outcome. This is in consonance with other studies showing no influence of sealer type on treatment outcome (16–19), even though the present study evaluated only cases with overfillings. Apart from many cytotoxic sealers and pastes used in the past, most of the contemporary filling materials exhibit significant cytotoxicity only before setting (24–26). In fact, even when sealers are kept within the canal space, an inflammatory response of varying intensity usually develops in the area where the sealers contact the vital apical and periradicular tissues (27). In case of overfillings, histologic sections show that the inflammatory response may be severe in the short-term (27). However, in time, most sealers lose their irritant components and become relatively inert (28, 29). In the long-term, in the absence of concurrent infection, proliferation of connective tissue infiltrated by a few scattered chronic inflammatory cells and multinucleated foreign body cells may be histologically observed around the extruded sealer (27).

Another important finding from this study was that overfillings were not associated with a poor outcome in teeth without apical periodontitis. This agrees with previous studies (10, 12) and lends credence to the concept that disease associated with overfillings is usually caused by a concomitant infection and not by cytotoxicity of the filling material (30). Overfillings are usually preceded by overinstrumentation, which may cause excessive enlargement and deformation of the apical foramen, making it difficult to achieve an appropriate apical adaptation of the filling material. In addition, teeth with apical periodontitis usually present with apical root resorption (27, 31), and this may lead to deformations that likewise compromise the apical filling quality. The lack of an adequate apical seal is problematic when leakage of tissue fluids and exudate into the canal reach residual bacteria to supply substrate for growth. Moreover, overinstrumentation inevitably displaces infected dentin and necrotic pulp debris into the periradicular tissues. Inoculated therein, bacteria embedded in debris may be physically protected from the host defense mechanisms and impair healing (32, 33).

TABLE 2. Outcome of the Endodontic Treatment of Teeth without Apical Periodontitis after Unintentional Extrusion of Different Sealers to the Periradicular Tissues

Sealer	Baseline *n*	1-year follow-up		2-year follow-up		>4-year follow-up		
		Healed	Diseased	Healed	Diseased	Healed	Diseased	Healed %
AH Plus	2	2	0	1	0	2	0	100
Apexit	4	1	0	1	0	4	0	100
Endomethasone	6	3	0	3	0	6	0	100
PCS	7	5	0	5	0	7	0	100
PCS EWT	10	8	0	10	0	10	0	100
Tubli-Seal	1	1	0	1	0	1	0	100

TABLE 3. Outcome of the Endodontic Treatment of Teeth with Apical Periodontitis after Unintentional Extrusion of Different Sealers to the Periradicular Tissues

Sealer	Baseline *n*	1-year follow-up			2-year follow-up			>4-year follow-up		
		Healed	Healing	Not healed	Healed	Healing	Not healed	Healed	Not healed	Healed %
AH Plus	18	4	6	1	11	3	2	14	4	78
Apexit	11	5	2	1	4	2	1	9	2	82
Endomethasone	9	2	2	2	2	3	1	8	1	89
PCS	21	4	1	4	5	2	4	14	7	67
PCS EWT	11	3	2	1	7	1	1	10	1	91
Tubli-Seal	5	2	1	0	2	1	0	4	1	80

On the basis of a few reports in the literature (8, 9), a foreign body reaction to extruded filling materials has been suggested as a possible cause of post-treatment apical periodontitis. Nonetheless, our findings indicating a 100% success rate for overfillings in teeth without apical periodontitis may suggest otherwise (ie, contemporary sealers when extruded through the apical foramen in small amounts, without causing gross overfilling, exert no significant toxicity or induce a foreign body reaction to an extent that is sufficient to cause post-treatment disease).

Although the extraradicular presence of the filling material may not be the direct cause of post-treatment disease, it has been suggested that healing may be substantially delayed in some cases (34). It was not the purpose of the present study to compare the healing process of teeth with or without overfillings because the latter were not included in the analyses. It is important to highlight that of 66 cases followed for more than 10 years, only 4 teeth had a change in outcome when compared with the 4-year recall. Although a case reverted from healed to diseased after 25 years (recurrent disease), 3 cases took more than 10 years to completely heal. If this long time lapsed until complete healing was a consequence of the extruded material cannot be inferred from the present study.

Although it was not the purpose of the present study, a common finding from the PCS, PCS EWT, and Tubli-Seal groups was that the sealer was not only removed from the periradicular tissues but also from the most apical part of the root canal. In terms of tissue repair, sealer dissolution in the apical canal may be advantageous because it creates space for connective tissue ingrowth, sometimes with deposition of new cementum layers to narrow the foramen and the apical canal lumen (35). On the other hand, sealer dissolution in the canal may provide space for fluid seepage and bacterial regrowth in the long-term, with risks for recurrent disease (36). Once again, the prognosis will depend on the presence of concomitant residual intracanal infection.

This study has its own limitations. First, the disappearance of extruded sealer on the radiograph does not automatically mean that it was completely removed from the periradicular tissues. The amount of material and/or its density may have been reduced to a point that it cannot be discerned on a radiograph. This condition has been described in histologic studies (27). Another limitation is the study's retrospective nature, which did not permit us to properly randomize cases for the type of sealer to be used nor to precisely establish the set points for organized recalls. In addition, in some cases, film holders could not be used to take radiographs, which precluded an analysis of the amount of material extruded and restricted our findings on "fate" to presence/absence data. However, because of the bidimensional nature of radiographs, quantification of the extruded material (perhaps by area) would be recognizably deficient and inappropriate.

In conclusion, the present study showed that not all extruded materials were removed from the periradicular tissues to the point that they were no longer visible on the radiograph; zinc oxide eugenol–based sealers were removed significantly faster than AH Plus and Apexit. However, only histologic analysis would eventually confirm their complete removal from the periradicular tissues. Treatment outcome is not significantly affected by the type of extruded sealer as long as the root canals are adequately treated. This does not mean that overfillings should be recommended because gross extrusion of filling materials has been reported to cause severe postoperative complications (37–39). Success rates in overfilled cases are significantly higher in teeth with no lesion in comparison with teeth with apical periodontitis.

Acknowledgments

The authors deny any conflicts of interest related to this study.

References

1. Siqueira JF Jr. *Treatment of Endodontic Infections*. London: Quintessence Publishing; 2011:313–40.
2. Ricucci D, Langeland K. Apical limit of root canal instrumentation and obturation, part 2. A histological study. Int Endod J 1998;31:394–409.
3. Schaeffer MA, White RR, Walton RE. Determining the optimal obturation length: a meta-analysis of literature. J Endod 2005;31:271–4.
4. Sjögren U, Hagglund B, Sundqvist G, Wing K. Factors affecting the long-term results of endodontic treatment. J Endod 1990;16:498–504.
5. Ricucci D, Russo J, Rutberg M, et al. A prospective cohort study of endodontic treatments of 1,369 root canals: results after 5 years. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:825–42.
6. Schilder H. Filling root canals in three dimensions. Dent Clin North Am 1967;11:723–44.
7. Muruzábal M, Erasquin J, DeVoto FCH. A study of periapical overfilling in root canal treatment in the molar of rat. Arch Oral Biol 1966;11:373–83.
8. Nair PN, Sjögren U, Krey G, Sundqvist G. Therapy-resistant foreign body giant cell granuloma at the periapex of a root-filled human tooth. J Endod 1990;16:589–95.
9. Ricucci D, Siqueira JF Jr, Bate AL, Pitt Ford TR. Histologic investigation of root canal-treated teeth with apical periodontitis: a retrospective study from twenty-four patients. J Endod 2009;35:493–502.
10. Sjögren U, Figdor D, Persson S, Sundqvist G. Influence of infection at the time of root filling on the outcome of endodontic treatment of teeth with apical periodontitis. Int Endod J 1997;30:297–306.
11. Byström A, Happonen RP, Sjögren U, Sundqvist G. Healing of periapical lesions of pulpless teeth after endodontic treatment with controlled asepsis. Endod Dent Traumatol 1987;3:58–63.
12. Lin LM, Skribner JE, Gaengler P. Factors associated with endodontic treatment failures. J Endod 1992;18:625–7.
13. Siqueira JF Jr, Rôças IN, Ricucci D, Hülsmann M. Causes and management of post-treatment apical periodontitis. Br Dent J 2014;216:305–12.
14. Fristad I, Molven O, Halse A. Nonsurgically retreated root filled teeth–radiographic findings after 20-27 years. Int Endod J 2004;37:12–8.
15. Augsburger RA, Peters DD. Radiographic evaluation of extruded obturation materials. J Endod 1990;16:492–7.
16. Ørstavik D, Qvist V, Stoltze K. A multivariate analysis of the outcome of endodontic treatment. Eur J Oral Sci 2004;112:224–30.
17. Huumonen S, Lenander-Lumikari M, Sigurdsson A, Ørstavik D. Healing of apical periodontitis after endodontic treatment: a comparison between a silicone-based and a zinc oxide-eugenol-based sealer. Int Endod J 2003;36:296–301.
18. Eriksen HM, Ørstavik D, Kerekes K. Healing of apical periodontitis after endodontic treatment using three different root canal sealers. Endod Dent Traumatol 1988;4:114–7.
19. Waltimo TM, Boiesen J, Eriksen HM, Ørstavik D. Clinical performance of 3 endodontic sealers. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001;92:89–92.

20. Strindberg LZ. The dependence of the results of pulp therapy on certain factors. Acta Odontol Scand 1956;14(Suppl 21):1–175.
21. Faria-Junior NB, Tanomaru-Filho M, Berbert FL, Guerreiro-Tanomaru JM. Antibiofilm activity, pH and solubility of endodontic sealers. Int Endod J 2013;46:755–62.
22. Schäfer E, Zandbiglari T. Solubility of root-canal sealers in water and artificial saliva. Int Endod J 2003;36:660–9.
23. Marin-Bauza GA, Silva-Sousa YT, da Cunha SA, et al. Physicochemical properties of endodontic sealers of different bases. J Appl Oral Sci 2012;20:455–61.
24. Spångberg LS, Barbosa SV, Lavigne GD. AH 26 releases formaldehyde. J Endod 1993;19:596–8.
25. Barbosa SV, Araki K, Spångberg LS. Cytotoxicity of some modified root canal sealers and their leachable components. Oral Surg Oral Med Oral Pathol 1993;75:357–61.
26. Ørstavik D, Mjör IA. Histopathology and x-ray microanalysis of the subcutaneous tissue response to endodontic sealers. J Endod 1988;14:13–23.
27. Ricucci D, Siqueira JF Jr. *Endodontology. An Integrated Biological and Clinical View*. London: Quintessence Publishing; 2013:239–91.
28. Langeland K. Root canal sealants and pastes. Dent Clin North Am 1974;18:309–27.
29. Spångberg LSW, Haapasalo M. Rationale and efficacy of root canal medicaments and root filling materials with emphasis on treatment outcome. Endod Topics 2002;2:35–58.
30. Siqueira JF Jr. Aetiology of root canal treatment failure: why well-treated teeth can fail. Int Endod J 2001;34:1–10.
31. Vier FV, Figueiredo JA. Prevalence of different periapical lesions associated with human teeth and their correlation with the presence and extension of apical external root resorption. Int Endod J 2002;35:710–9.
32. Yusuf H. The significance of the presence of foreign material periapically as a cause of failure of root treatment. Oral Surg Oral Med Oral Pathol 1982;54:566–74.
33. Ricucci D, Siqueira JF Jr, Lopes WS, et al. Extraradicular infection as the cause of persistent symptoms: a case series. J Endod 2015;41:265–73.
34. Molven O, Halse A, Fristad I, MacDonald-Jankowski D. Periapical changes following root-canal treatment observed 20-27 years postoperatively. Int Endod J 2002;35:784–90.
35. Ricucci D, Lin LM, Spångberg LS. Wound healing of apical tissues after root canal therapy: a long-term clinical, radiographic, and histopathologic observation study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:609–21.
36. Vieira AR, Siqueira JF Jr, Ricucci D, Lopes WS. Dentinal tubule infection as the cause of recurrent disease and late endodontic treatment failure: a case report. J Endod 2012;38:250–4.
37. Gonzalez-Martin M, Torres-Lagares D, Gutierrez-Perez JL, Segura-Egea JJ. Inferior alveolar nerve paresthesia after overfilling of endodontic sealer into the mandibular canal. J Endod 2010;36:1419–21.
38. Brkic A, Gurkan-Koseoglu B, Olgac V. Surgical approach to iatrogenic complications of endodontic therapy: a report of 2 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;107:e50–3.
39. Alves FR, Coutinho MS, Gonçalves LS. Endodontic-related facial paresthesia: systematic review. J Can Dent Assoc 2014;80:e13.