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ORIGINAL ARTICLE

Clinical efficacy of root canal treatment at 2 years using a new ready-to-use injectable calcium silicate-based sealer: A multicentric randomised controlled trial

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Abstract

Aim: Calcium silicate-based sealers (CSSs) have gained popularity in endodontic applications primarily due to their biological properties and ease of use. This study aimed to assess the 24-month efficacy and safety of root canal treatment using a new injectable CSS, BioRoot™ Flow, and to demonstrate the non-inferiority compared to the established hand-mixed BioRoot™ RCS.

Methodology: This was a multicentric, prospective, randomised, assessor-blinded, controlled, non-inferiority trial (ClinicalTrials.gov: NCT04757753). Patients requiring a primary or a secondary root canal treatment on a single or multi-rooted tooth were block randomly assigned to BioRoot Flow or BioRoot RCS groups. The primary outcome was the 24-month success rate based on clinical and radiological criteria. Secondary outcomes included the 6- and 12-month success rates based on similar radiological and clinical criteria, quality of obturation, resorption of extruded material in case of overfilling assessed at 6, 12 and 24 months, post-operative pain measured using the Visual Analog Scale (VAS) at baseline, 12 h, 24 h, 48 h, 72 h and 7 days, and occurrence of adverse events. A subgroup analysis was also performed based on the type of treatment and on the presence or absence of apical periodontitis (AP) at baseline. Non-inferiority between materials was assessed using Dunnett and Gent's Chi-squared (χ^2) test, based on an initial hypothesis with a non-inferiority margin set at 13%, an 80% power and a 5% one-sided alpha risk. Investigators and patients were not blinded to the assigned medical device. Two qualified evaluators performed a blinded independent central review of the retro-alveolar radiographs.

Results: A total of 160 patients with a mean age of 48 years were treated (77 in BioRoot Flow and 83 in BioRoot RCS). The 24-month follow-up rate was 85.6%. The overall 24-month success rates were 86.6% and 87.7% ($p = .0195$), respectively. No significant differences were observed between the groups regarding any of the considered secondary outcomes. No adverse events were reported.

Conclusion: This study demonstrated the non-inferiority of the new injectable CSS (BioRoot Flow) compared to the previous hand-mixed version (BioRoot RCS) in terms of efficacy and safety, supporting the implementation of the new material in clinical practice.

KEYWORDS

BioRoot TM, calcium silicate-based sealer, endodontics, RCT, root canal filling, root canal treatment

INTRODUCTION

While it is widely acknowledged that the success of root canal treatment depends on numerous factors, recent studies have emphasised the need to simplify this complex picture by narrowing the list down to a few biologically oriented principles (Gulabivala & Ng, 2023; Van Nieuwenhuysen et al., 2023). This is in line with both the original Clinical Practice Guidelines (European Society of Endodontology, 2006) and the most recent S3-level guidelines (Duncan et al., 2023) from the European Society of Endodontology, which provide key recommendations focussing on what is considered the essential steps of root canal treatments to maximise their success. These steps include proper diagnosis and treatment decision-making, followed by adequate root canal preparation using contemporary instruments, copious irrigation involving sodium hypochlorite (NaOCl) and ethylenediaminetetraacetic acid (EDTA), and final obturation with gutta-percha (GP) combined with a sealer. Root canal filling techniques vary and include cold lateral compaction, warm vertical compaction, carrier-based systems and the single-cone technique. There are also a variety of sealers available, including epoxy resin, zinc oxide eugenol (ZOE) or calcium silicate (CS). The final step of treatment, obturation, is generally considered one of the most critical factors for long-term success, as reinfection of the root canal system due to bacterial leakage is widely regarded as a major cause of endodontic failure (Siqueira, 2001). Leakage can occur at the different interfaces between the GP, sealer and dentine (Veríssimo & do Vale, 2006).

Thus, an ideal root canal sealer material should combine certain characteristics such as bioactivity, biocompatibility, long-term and hermetic sealing ability and good operating performance (Dong & Xu, 2023).

While standard sealers such as epoxy or ZOE formulations have been used effectively for decades, calcium silicate-based sealers (CSSs) have gained popularity in endodontic applications over the last decade due notably to their biological properties and ease of use. With the introduction of CSSs, root canal treatments have experienced a significant shift, positioning them as a highly effective alternative in modern endodontic practice. They show similar or better performance compared to resin-based sealers, particularly in terms of physicochemical properties and no or less cytotoxicity (Chopra et al., 2021; Silva Almeida et al., 2017), while displaying very interesting characteristics such as excellent biocompatibility and bioactivity (Eskandari et al., 2022; Hench, 1991; Raghavendra et al., 2017; Wang, 2015). These improved biological and physicochemical properties were reported as the main reasons for practitioners to use these CSSs (Guivarc'h et al., 2020).

Initially, they were formulated as a powder to be mixed with a water-based liquid. Various ready-to-use, injectable versions were then developed to improve the galenic forms as the consistency was previously highly operator-dependent. These pre-mixed formulations have rapidly gained popularity, particularly among general dental practitioners (Guivarc'h et al., 2020), for their simplicity of use and time-saving benefits.

However, while in-vitro and animal studies have largely demonstrated their comparability with conventional formulations in most aspects, some studies have also identified potential concerns regarding certain cements, particularly their solubility (Raman & Camilleri, 2024; Silva Almeida et al., 2017) and the need for sufficient fluid in a dry canal to ensure proper hydration (Cardinali & Camilleri, 2023; Zancan et al., 2021).

In this context, clinical data is critically needed to demonstrate their long-term treatment efficacy. A recent systematic review reported similar outcomes when comparing these pre-mixed CSSs to standard sealers (Zamparini et al., 2024), but also identified flaws in the available studies, notably inconsistencies in reporting and short-term duration. Other clinical studies have shown promising results regarding these pre-mixed CSSs, but were either retrospective (Chybowski et al., 2018; Kangseng et al., 2025; Lepure et al., 2024; Radwanski et al., 2024) or prospective without controls (Spinelli et al., 2024). As concluded by Zamparini et al., more robust prospective long-term data are therefore required. To date, there has been no formal randomised comparison

with a conventional powder-liquid formulation. The latter, however, was demonstrated to be equally efficient to ZOE and epoxy-resin sealers for up to 4 years (Bardini et al., 2025, 2021; Zavattini et al., 2020).

This study thus sought to evaluate the 24-month efficacy and safety of root canal treatment with the new ready-to-use injectable CSS BioRoot™ Flow and to demonstrate its non-inferiority to a control material, i.e. BioRoot™ RCS.

MATERIALS AND METHODS

Ethical consideration and study design

This study was a multicentric, prospective, randomised, assessor-blinded, controlled trial conducted from November 2020 to September 2023. It was carried out in six private dental practices and one university hospital with three endodontics-only practitioners and four general practitioners. This randomised clinical trial has been written according to Preferred Reporting Items for Randomised Trials in Endodontics (PRIRATE) 2020 guidelines (Nagendrababu et al., 2020). The study was approved by ethics committees and local authorities prior to patient enrollment (ID-RCB: 2020-A01790-39-PP, CEFH: 2020/07OCT/492) and was conducted in accordance with good clinical practice guidelines and the Declaration of Helsinki. The study was registered on ClinicalTrials.gov (NCT04757753). All participants signed an informed consent to participate in the study.

Sample size calculation

Based on the assumption that there would be no difference in success rate at 24 months between the two filling materials, BioRoot Flow and BioRoot RCS, and that the expected success rate of BioRoot RCS after initial treatment and retreatment would be 90% (Chybowski et al., 2018; Eyuboglu et al., 2017; Zavattini et al., 2020), a minimum of 66 subjects per group had to be included to demonstrate non-inferiority of BioRoot Flow compared to BioRoot RCS with 80% power, 5% one-sided alpha risk, and tolerating a 13% difference in success rate (Eyuboglu et al., 2017; Ng et al., 2008, 2007). Including an additional 20% of patients to account for possible loss during follow-up or withdrawal from the study, the required number of patients to be included was 80 in each group or 160 patients in total. Sample size calculation was performed using JMP® version 17.0.0 (JMP Statistical Discovery LLC).

Eligibility of participants

Participants were selected according to the inclusion and exclusion criteria summarised in Table 1. Recruitment took place between November 2020 and July 2021. Patients were diagnosed based on pain history, response to sensitivity tests, palpation, percussion and retroalveolar radiographs.

Randomisation

Participants were randomly assigned to the two groups, BioRoot Flow and BioRoot RCS, using a computer-generated block randomisation list created with Sealed Envelope Ltd. Randomisation was stratified by indication for root canal treatment (i.e. initial treatment or retreatment), with the maximum expected proportion of retreatment set at 30%. Between 22 and 24 patients were to be included in each centre.

Blinding and radiographic evaluation

The radiographic assessment was conducted by two independent qualified evaluators who performed a centralized review of retro-alveolar radiographs taken preoperatively, at baseline immediately after root canal treatment, and at 6, 12 and 24 months. They were trained in two key areas prior to the evaluation. First, they were trained to detect apical lesions in 160 root canals. After the first reading, two additional assessments were made, resulting in a final agreement rate of 93%. Second, they were trained to evaluate density and identify voids in the filling material, reaching a 97% agreement rate on the first reading. The evaluators visually assessed the following criteria:

- Level of obturation (complete filling, underfilling, or overfilling): complete filling was defined as being 0.5–2 mm short of the radiographic apex.
- Quality of obturation: The quality of the obturation was assessed by evaluating the density of the obturation and the presence/absence of voids. Sufficient radiopacity was defined as the adequate visibility of the materials on radiographs, allowing clear identification of the filling material (Yes or No)
- Resorption of extruded material in the case of overfilling (Yes or No)
- Any change in the size of periapical radiolucency (reduction, stabilisation or increase)

The two evaluators were blinded to the clinician, dental treatment centre, patient, indication and treatment group. The Kappa–Cohen test was used for examiner

TABLE 1 Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Male or female, age > 18 years old	Patient with one or more documented contraindications to endodontic treatment
Patient requiring a primary or a secondary root canal obturation on a single or multi-rooted tooth	Contraindication to the use of calcium silicate root canal sealer, such as an immature tooth or a known hypersensitivity to one component of the sealer formula
Patient geographically stable and/or regularly followed in the dental office, with a follow-up period of 24 months	Endodontic treatment on tooth with a calcified canal
Patient who received information and gave written consent (signed informed consent form)	Endodontic treatment on a tooth with suspected perforation
Subject affiliated with a health insurance system, or is a beneficiary	Patient with an uncontrolled systemic disease such as diabetes or thyroid disorders or with an immunocompromised condition or who has undergone radiation therapy to the jaw
	Patient suffering from uncontrolled active periodontitis
	Concurrent participation in other interventional research

calibration, following the recommendations described by Landis and Koch (1977), with a weighted kappa value of $k = 0.81$. Investigators and patients were not blinded to the assigned medical device due to the different presentation and use of the two products.

Clinical procedure

After local anaesthesia was administered, a rubber dam was placed. Root canal treatments were performed in accordance with the applicable Clinical Practice Guidelines (European Society of Endodontology, 2006), allowing flexibility for the practitioner. The protocol varied in terms of the type of rotary instruments used and the irrigation activation protocols. The concentration of NaOCl used for root canal disinfection ranged between 3% and 6%. For Bioroot Flow, the canal was dried without excessive dehydration and then the material was injected 2 mm from the apex, gradually filling the canal until complete obturation before the GP was placed.

The BioRoot RCS mixture was prepared according to the manufacturer's instructions and inserted into the canal using a lentulo spiral or by coating GP cones. Aside from the sealer, practitioners were free to choose their preferred obturation method, with root canals being obturated either using the single-cone technique or the cold lateral condensation technique. Root canal treatments were completed in one session or in two sessions if bleeding, pus, or inflammatory exudate prevented proper drying of the root canal.

Assessment of treatment outcome

Primary outcome

The 24-month success rate of endodontic treatment was based on both radiological criteria evaluated by two independent reviewers and clinical criteria assessed by the investigator.

According to the criteria defined in the recent S3-level guidelines by the ESE (Duncan et al., 2023), treatment success was defined as a combination of clinical (absence of pain, tenderness and swelling) and radiographical (radiographic evidence of disappearance or reduction of periapical radiolucency) criteria. This corresponds to what Ng et al. described as 'loose' success criteria (Ng et al., 2007).

Treatment failure was defined as non-functional teeth associated with clinical signs (pain, swelling, sinus tract, tooth extraction due to endodontic failure, etc.) and/or symptoms related to the endodontic treatment and/or with the stagnation, appearance, or enlargement of a periapical radiolucency.

Secondary outcomes

- 6- and 12-month success rate of endodontic treatment based on radiological and clinical criteria;
- Level and quality of obturation as assessed by the evaluators;

- Pain assessment: Pre- and post-operative pain experienced by the patient was measured using the Visual Analogue Scale (VAS) ranging from 0 to 100 mm at baseline, 12 h, 24 h, 48 h, 72 h and 7 days. The maximum post-operative pain felt between T0 and 7 days and the time of occurrence of the maximum pain were also recorded. Patients used pain diaries to document pain intensity and progression throughout the follow-up periods. The proportion of patients who took oral analgesics or anti-inflammatory medication during the first 7 days after the procedure was recorded;
- Adverse events: The number, severity and causality of adverse events during and after root canal treatment were recorded to assess safety.

Detailed information can be found in the Data S1.

Statistical analysis

Statistical analyses were run using JMP® version 17.0.0 (JMP Statistical Discovery LLC).

For the primary outcome, the Dunnett and Gent's chi-squared test was used to assess non-inferiority between the groups regarding the difference in 24-month success rates, with 80% power and 5% one-sided alpha risk. The hypothesis was that BioRoot Flow would be non-inferior to BioRoot RCS, with a non-inferiority margin set at 13% or 0.13. Confidence intervals were used to evaluate the primary outcome within subgroups based on baseline characteristics: presence of apical radiolucencies and type of treatment (initial or retreatment). The lower limit of these 90% confidence intervals was compared to the non-inferiority limit of 13% (value: −0.13).

For the secondary outcomes, comparisons between the groups at each time point were performed using Pearson's chi-squared test or Fisher's exact test for nominal variables and the Wilcoxon rank-sum test for quantitative variables.

RESULTS

A total of 164 patients were screened for eligibility and 160 patients were enrolled: 77 in the BioRoot Flow group and 83 in the BioRoot RCS group (Figure 1). Their mean age was 48 years (range: 18 to 82 years) and M/F ratio of 52%/48%. The proportion of initial treatment and retreatment corresponded to the initial hypothesis target (71% vs. 29%, respectively). Preoperative pulp and periapical diagnoses were similar in both groups. At baseline, 37.5% of teeth were symptomatic and 43.1% of teeth exhibited a periapical radiolucency (Table 2).

The single cone technique was used in 85.0% of cases and the cold lateral condensation technique in 15.0%. Root canal treatment was performed under a microscope in 41.6% and 43.4% of the cases in the BioRoot Flow and BioRoot RCS groups, respectively.

Of the 160 patients, 150 patients were seen at the 6-month follow-up, 143 at the 12-month follow-up, and 137 at the 24-monthfollow-up. 23 patients discontinued the study prematurely (11 in the BioRoot Flow group, 12 in the BioRoot RCS group). Of these, three patients had treatment failure and were considered as such in the 24-month success rate evaluation (Figure 1).

Primary outcome

At 24 months post-treatment, the overall success rate was 86.6% in the BioRoot Flow group and 87.7% in the BioRoot RCS group (non-inferiority demonstrated; $p = .0195$).

Secondary outcomes

No significant difference was observed between the two sealers in terms of success rate of root canal at the 6- and 12-month follow-up visits (Table 3).

Additionally, there was no significant difference in treatment success between the sealer subgroups at 24 months (Table 4; Figure 2).

Radiographic evaluation

Radiological evaluation of the canal obturation showed a satisfactory and stable quality of the root canal obturation for both sealers BioRoot Flow and BioRoot RCS sealers over the 24-month follow-up period. Radiopacity was sufficient for more than 95% of teeth and the presence of voids in the filling material was low (3%) for BioRoot Flow and around 8% for BioRoot RCS ($p = .4431$). At baseline, material extrusion was observed in 42.9% of cases in the BioRoot Flow group (33/77) and 28.9% in the BioRoot RCS group (24/83). At 6 months, the extruded material remained present in 84.8% (28/33) of cases in the BioRoot Flow group and 70.8% (17/24) in the BioRoot RCS group. At 12 months, it was observed in 84.4% (27/32) and 69.6% (16/23) of cases, respectively, and at 24 months, in 83.9% (26/31) and 71.4% (15/21) of cases, respectively.

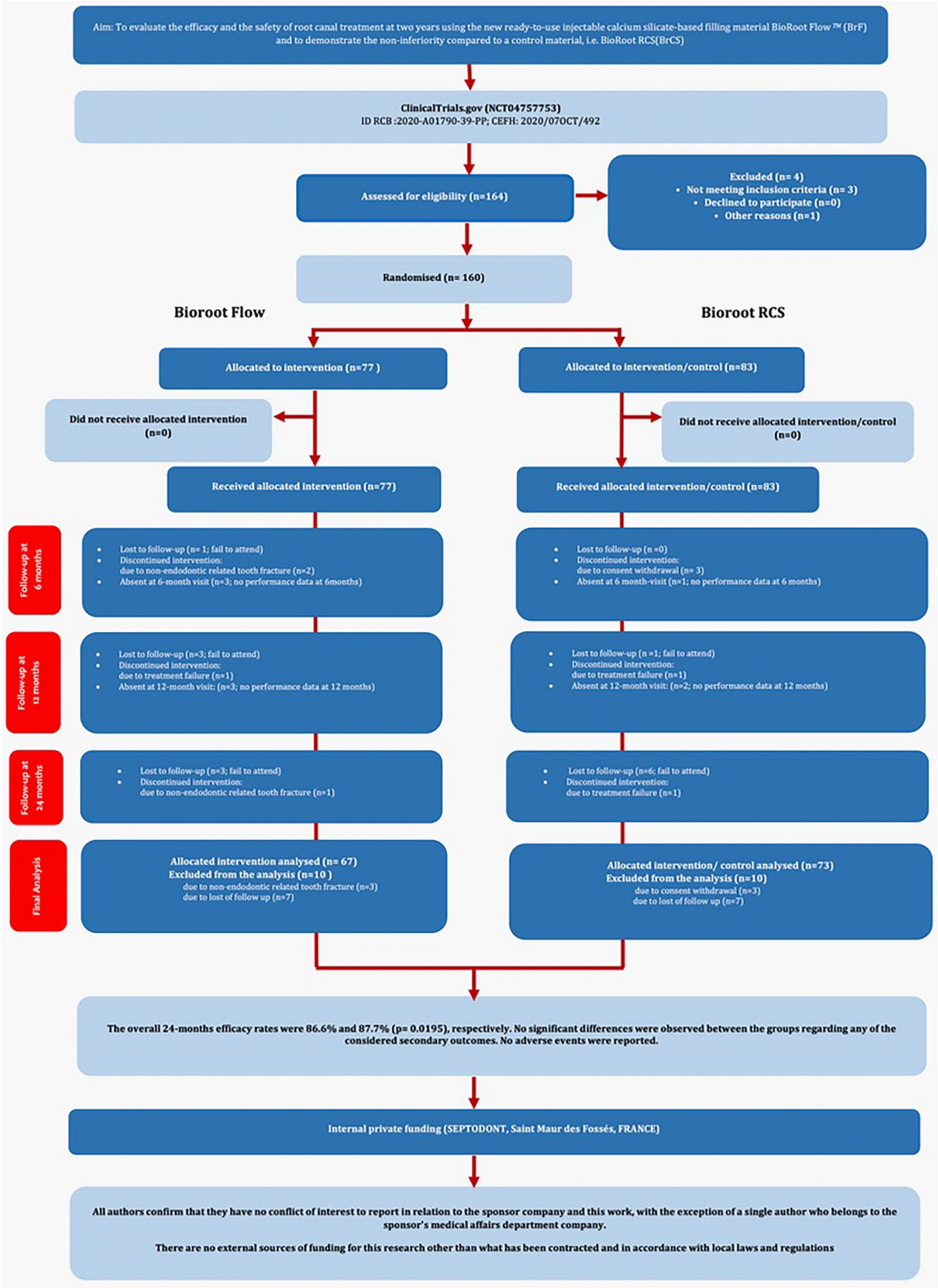

FIGURE 1 PRIRATE study flowchart.

Pain assessment

Mean and median preoperative pain values were low (mean = 6.5 ± 15.7 mm; median = 0) in 144 out of 160 patients who completed the pain diary, resulting in a response rate of 90.0%. The mean maximum post-operative pain values (16.8 ± 22 mm) were observed approximately 12 h after root canal obturation (146/160, 91.3%). After 3 days, the mean pain values were 3.3 ± 9.7 mm (146/160, 91.3%), and there was no pain on day 7 (mean:

TABLE 2 Baseline demographic and clinical features of patients in the study groups.

Characteristics		BioRoot flow *N* = 77	BioRoot RCS *N* = 83	Total *N* = 160
Age at inclusion (years old)	Mean	51.0 ± 16.1 [19.7; 81.3]	46.3 ± 16.3 [18.3; 81.9]	48.5 ± 16.3 [18.3; 81.9]
Sex	Female	31 (40.3%)	46 (55.4%)	77 (48.1%)
	Male	46 (59.7%)	37 (44.6%)	83 (51.9%)
Tooth arch	Maxilla	40 (51.9%)	52 (62.7%)	92 (57.5%)
	Mandible	37 (48.1%)	31 (37.3%)	68 (42.5%)
Tooth type	Incisor	8 (10.4%)	2 (2.4%)	10 (6.3%)
	Canine	3 (3.9%)	5 (6.0%)	8 (5.0%)
	Premolar	22 (28.6%)	31 (37.3%)	53 (33.1%)
	Molar	44 (57.1%)	45 (54.2%)	89 (55.6%)
Number of canals to treat	1 canal	23 (29.9%)	22 (26.5%)	45 (28.1%)
	2 canals	10 (13.0%)	16 (19.3%)	26 (16.3%)
	3 canals	26 (33.8%)	24 (28.9%)	50 (31.3%)
	4 canals	17 (22.1%)	20 (24.1%)	37 (23.1%)
	5 canals	1 (1.3%)	1 (1.2%)	2 (1.3%)
Type of endodontic treatment	Initial	55 (71.4%)	59 (71.1%)	114 (71.3%)
	Retreatment	22 (28.6%)	24 (28.9%)	46 (28.8%)
Pulp diagnosis of the tooth among initial treatment	Irreversible pulpitis	14 (25.5%)	11 (18.6%)	25 (21.9%)
	Necrotic pulp	28 (50.9%)	31 (52.5%)	59 (51.8%)
	Living pulp with root canal treatment indication (Prognosis of unfavourable pulp vitality before restorative procedure or Probability of pulp exposure during coronal restoration)	13 (23.6%)	17 (28.8%)	30 (26.3%)
Symptomatic tooth	Yes	28 (36.4%)	32 (38.6%)	60 (37.5%)
	No	49 (63.6%)	51 (61.4%)	100 (62.5%)
Periapical status of the tooth (radiograph)	Presence of periapical radiolucency	34 (44.2%)	35 (42.2%)	69 (43.1%)
	Absence of periapical radiolucency	43 (55.8%)	48 (57.8%)	91 (56.9%)

0.6 ± 1.5 mm) (126/160, 78.8%) (Figure 3). No significant difference was found between the two groups ($p = .8382$). Response rates refer to patients who completed the pain assessment at each time point.

Around half of the patients took at least one oral analgesic during the first 7 post-operative days. The most frequently taken analgesic was paracetamol (60%; mean cumulative dose = 2.6 ± 2.7 g), followed by ibuprofen (31%; mean cumulative dose = 1 ± 0.9 g). No adverse events related to the use of these materials were reported in this study.

DISCUSSION

The authors of this study believe that it is the first randomised controlled clinical trial to evaluate the efficacy and the safety of root canal treatment 2 years after root canal treatment including a ready-to-use injectable CSS. A 2-year follow-up is in line with the recommendations of the ESE (European Society of Endodontology, 2006), which considers 1 year to be the minimum duration for evaluating the success of endodontic treatment (Duncan et al., 2021, 2023; European Society of Endodontology, 2006). It also takes into account data suggesting that when complete healing occurs, it does so in the majority of cases (> 80%) within the first 2 years post-treatment (Orstavik, 1996).

The results of the study showed that the treatment success rates were similar between the new material and the powder-liquid control, with high success rates in both cases (86.6% and 87.7%, respectively). No material-related adverse events were reported. With equal efficacy and safety outcomes, the new formulation enhances ease of use for practitioners.

There are very few studies investigating the success rates of CSSs, in particular those involving the new generation of ready-to-use injectable sealers. Among the available data, several studies have shown promising

TABLE 3 Primary outcome analysis by 'loose' criteria at 6 months, 12 months and 24 months.

Outcomes	M6				M12				M24				Non-inferiority comparison Chi-square of Dunnet and Gent
	BioRoot flow $N=71$	BioRoot RCS $N=79$	Total $N=150$	Comparison	BioRoot flow $N=68$	BioRoot RCS $N=77$	Total $N=145$	Comparison	BioRoot flow $N=67$	BioRoot RCS $N=73$	Total $N=140$	
Success rate	61 (85.9%)	69 (87.3%)	130 (86.7%)	$p=.7975$ Chi-square test	61 (89.7%)	67 (88.2%)	128 (88.9%)	$p=.7679$ Chi-square test	58 (86.6%)	64 (87.7%)	122 (87.1%)	$p=.0195$

results for CSSs in terms of success rate. Chybowski et al. described the clinical outcomes of using the single-cone technique with a CSS in 307 teeth treated between 2009 and 2015, over a follow-up period of 30 months. The success rate was 90.9% using 'loose' criteria (Chybowski et al., 2018). On the other hand, Zavattini et al. compared the use of a CSS using a single-cone obturation technique and epoxy-based sealer in combination with warm vertical compaction. The results at 12 months showed a similar proportion of successful cases compared to warm vertical condensation and epoxy-based sealer (Zavattini et al., 2020). Similarly, Kangseng et al. recently found no significant difference in success rates between CSSs and epoxy resin-based sealers with a mean follow-up of 15 months (Kangseng et al., 2025). However, the study designs were either retrospective or prospective without randomisation. The present work therefore fills the gap and provides more robust evidence of the reliability of CSS technology, including a new ready-to-use injectable formulation.

The present study presents several advantages over the available historic data. First, its randomised and prospective nature, with systematic control of the cases and a high percentage of follow-up at 2 years (85.6%). Second, the work included a variety of cases, with both primary treatments and retreatments, cases with and without periapical lesions, as well as a diversity of practitioners, both general dentists and specialized endodontists. Patients with contraindications to endodontic treatment or CSSs and those with complex dental conditions (e.g. calcified canals, suspected perforations) and uncontrolled systemic diseases or active periodontitis were excluded from the study to minimise risks and confounding factors.

It is very interesting and promising to observe that the presence of periapical radiolucencies in this work did not result in significantly lower success rates, although this criterion was repeatedly identified as a variable affecting root canal treatment success in the large long-term prospective cohort studies (Ng et al., 2007; Ricucci et al., 2011; Van Nieuwenhuysen et al., 2023). This may indicate a beneficial effect of these CSSs in terms of promoting periapical healing and remineralisation, thereby supporting their bioactive characteristics and good biological properties. Indeed, several in vitro studies demonstrated that both BioRoot RCS and BioRoot Flow exhibit good cytocompatibility with Human Periodontal Ligament Stem Cells (hPDLSCs) and induce osteo/cementogenic differentiation. They also downregulate the inflammatory cytokine IL-6 and significantly influence cell mineralisation. They penetrate dentinal tubules, enhancing root canal filling durability. In addition, their alkaline pH (>10) is unfavourable to bacteria, which might have survived despite the irrigation protocol of the

TABLE 4 Primary outcome analysis by subgroup.

Subgroup 1: Initial treatment	**BioRoot Flow (*N* = 47)**	**BioRoot RCS (*N* = 53)**	**Total (*N* = 100)**	**Comparison of success rate diff [90% CI]**
Success at 24 months	42 (89.4%)	47 (88.7%)	89 (89.0%)	0.7% [−9.6%; 11.0%]
Subgroup 1: Retreatment	**BioRoot Flow (*N* = 20)**	**BioRoot RCS (N = 20)**	**Total (*N* = 40)**	**Comparison of success rate Diff [90% CI]**
Success at 24 months	16 (80.0%)	17 (85.0%)	33 (82.5%)	−5.0% [−24.7%; 14.7%]
Subgroup 2: presence of periapical lesion at baseline	**BioRoot Flow (*N* = 30)**	**BioRoot RCS (N = 30)**	**Total (*N* = 60)**	**Comparison of success rate Diff [90% CI]**
Success at 24 months	25 (83.3%)	27 (90.0%)	52 (86.7%)	−6.7% [−21.0%; 7.7%]
Subgroup 2: absence of periapical lesion at baseline	**BioRoot Flow (*N* = 37)**	**BioRoot RCS (*N* = 43)**	**Total (*N* = 80)**	**Comparison of success rate Diff [90% CI]**
Success at 24 months	33 (89.2%)	37 (86.0%)	70 (87.5%)	3.1% [−8.9%; 15.2%]

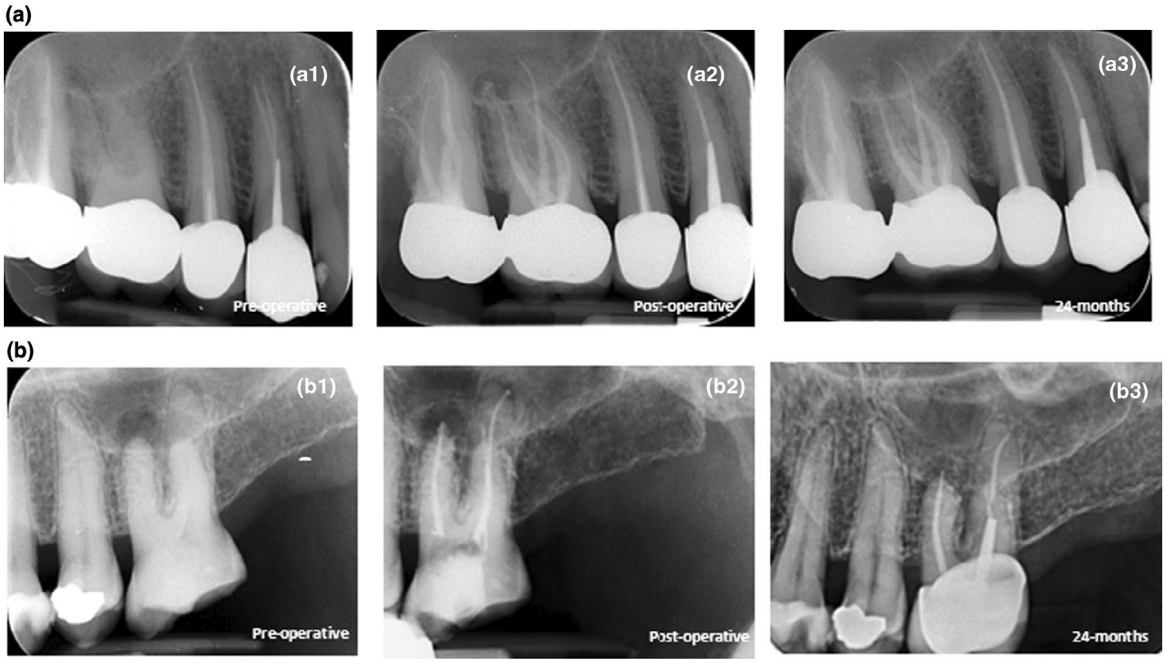

FIGURE 2 Radiological follow-up: (a) Successful treatment: Root canal treatment on the upper right first molar (#16) with an apical lesion on the disto-buccal root apex. The 24-month recall radiograph highlights a full healing of the lesion: (A1) pre-operative radiograph, (A2) Post-operative radiograph, (A3) 24 months post-operative recall radiograph. (b) Failure case: Root canal treatment of an upper left first molar (#26) with two apical lesions (mesio-buccal root and palatal root). The 24-month recall highlights the healing of the lesion on the palatal root, but a persistence of the lesion on the mesio-buccal root. This case was considered a failure. (B1) pre-operative radiograph, (B2) Post-operative radiograph, (B3) 24-month post-operative recall radiograph.

root canals (Camps et al., 2015; Eskandari et al., 2022; Sanz et al., 2024). These specific biological properties of CSS are due to the presence of CS, whose setting reaction leads to hydration by-products such as hydroxyl and calcium ions and calcium hydroxide followed by a precipitation reaction with calcium phosphate leading to hydroxyapatite formation, which enhances the interface between the sealer and the root dentin and increases the pH of the medium (Al-Haddad & Aziz, 2016; Camilleri, 2020).

However, further clinical studies should be carried out to assess the bioactivity of CSSs histologically using biomarkers such as calcium or other alternative methods.

Moreover, 37.5% of patients in this study had a symptomatic tooth at inclusion, but the mean post-operative pain was low in both groups, with no pain reported by Day 7. While contrasting results are available in the literature regarding this aspect, there is evidence correlating post-operative pain with the use of specific endodontic

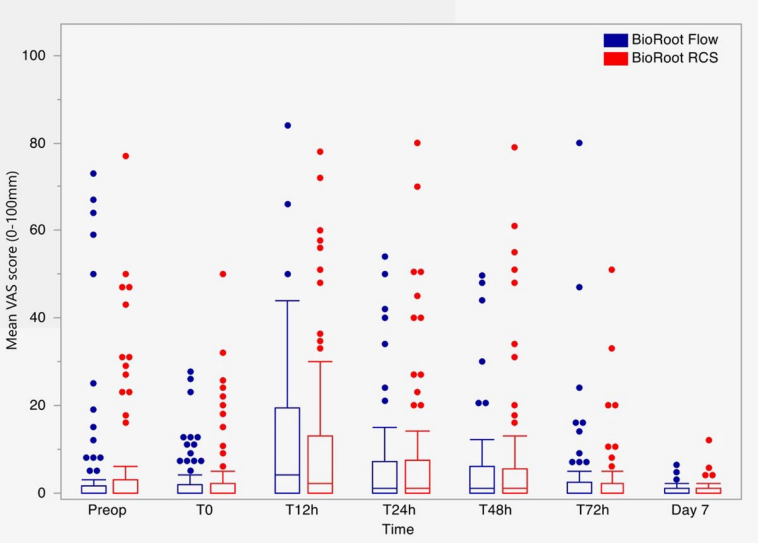

FIGURE 3 Description of pre-and post-operative pain (mean ± SD).

sealers. The current study results support an encouraging association with the CSS category. A systematic review and meta-analysis recently suggested that the use of CSSs may positively affect the intensity of post-operative pain and analgesic intake compared with resin-based sealers (Mekhdieva et al., 2021). Given that several factors may be related to endodontic post-operative pain, further studies with specific questions about these factors should be performed.

Complete healing or lesion reduction was considered a successful treatment because it is considered to be a realistic evaluation of success in normal practice. The authors of this work believe that using criteria closest to pragmatic day-to-day practice is therefore more useful to practitioners. According to Ng et al., strict radiological criteria correspond to the absence of apical radiolucency, and reduction in the size of radiolucency is considered a loose criterion (Ng et al., 2007). According to Patel, it could be unrealistic to achieve complete healing in all cases even if it may be ideal (Patel et al., 2019). Moreover, Orstavik et al. found that in some cases, it took 4 years to achieve complete healing of preoperative chronic apical periodontitis, while at least 89% of all healing roots showed signs of initiated but incomplete healing after 1 year. Reversal of the healing process was observed in only one case (Orstavik, 1996). These rates are within the thresholds for primary and secondary endodontic treatment success (Ng et al., 2007, 2008).

This study provides valuable insights, but certain factors should be considered. Blinding of the practitioners was not possible due to the different formulations of the products—BioRoot RCS in powder and liquid form and BioRoot Flow as a pre-mixed syringe. This, in turn, predisposes the study to detection bias for patient-rated outcomes such as post-operative pain, as patient awareness of the treatment may influence their perception. However, this was not the aim of the study.

The use of two obturation techniques could also introduce a confounding variable that may affect the study outcomes. However, the distribution of obturation techniques was the same for both groups. The single-cone technique was used in 85% of cases, and the cold lateral condensation technique was used in 15% of cases. The success rate was 89.5% (57 out of 67 cases) with BioRoot Flow/single cone obturation technique and 91.8% (61 out of 73 cases) with BioRoot RCS/single cone obturation technique.

The success rate was 100.0% (10 out of 67 cases) with BioRoot Flow/lateral condensation technique and 88.5% (12 out of 73 cases) with BioRoot RCS/ lateral condensation technique.

The most recent randomised clinical trial by Bardini et al. (2025) assessed the outcomes of non-surgical root canal treatment by comparing a CSS with the single-cone technique to a ZOE sealer with warm vertical compaction. After 4 years of follow-up, both treatments had similar success rates of 92.1% and 86.2%, respectively, for the CSS using the single-cone technique and the ZOE sealer using warm vertical compaction. These findings suggest comparable long-term results between the two techniques.

Finally, it is important to highlight that the single-cone obturation technique using CSSs is expected to simplify and expedite the obturation procedure, particularly in cases of restricted access such as limited mouth opening or posterior teeth, compared to thermoplasticised GP obturation techniques (Sfeir et al., 2021). The main difference between BioRoot Flow and BioRoot RCS is the method of application: while BioRoot Flow is presented in a ready-to-use syringe, BioRoot RCS requires manual mixing of powder and liquid, which can extend chair time,

introduce inconsistencies and render the procedure more operator-dependent. Therefore, the main technical difficulties with a ready-to-use sealer could be limited to the intracanal sealer placement and GP cone insertion, possibly making the procedure easier and more predictable.

Further studies with longer follow-up periods are needed to investigate the long-term success of CSSs and to identify the factors influencing success rates over time. Future research should also focus on comparing the outcomes of CSSs used by endodontists versus general practitioners.

CONCLUSION

This randomised controlled multicentric study including general practitioners and endodontists demonstrates the efficacy of calcium silicate-based materials. Based on the findings and within the limitations of this study, the new injectable CSS 'BioRoot Flow' resulted in a level of efficacy and safety comparable to the established hand-mixed BioRoot RCS, supporting the implementation of the new material in clinical practice.

AUTHOR CONTRIBUTIONS

Stéphane Simon coordinated the study and contributed to the study design, supervision of data acquisition, critical review of the manuscript, and final approval. Julien Beauquis, Hugues Colombel, Audrey Dorn, Valentin Marchi, Sébastien Robert, Grégoire Souleau, and Nadia Ravalec contributed to data acquisition, manuscript review, and approval. Florent Huguet-Jaime and Karine Chazaud contributed as independent evaluators to data interpretation, manuscript review, and approval. Anne-Laure Serandour, as clinical project manager (CRO), contributed to study design, data interpretation, and manuscript review and approval. Julian Leprince was involved in data acquisition, interpretation and analysis, as well as critical review and final approval of the manuscript. Nabila Ournid led the manuscript drafting and contributed to data interpretation, analysis, critical review, and final approval. All authors agree to be accountable for the integrity and accuracy of the work.

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CONFLICT OF INTEREST STATEMENT

All authors confirm that they have no conflict of interest to report in relation to the sponsor company and this work, with the exception of a single author who belongs to the sponsor's medical affairs department company. There are no external sources of funding for this research other than what has been contracted and in accordance with local laws and regulations.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in Clinicaltrial.gov at https://clinicaltrials.gov/study/NCT04757753?term=PA1704&rank=1, reference number NCT04757753.

ETHICS STATEMENT

The study was approved by relevant ethics committees and local authorities prior to patient enrollment (ID-RCB: 2020-A01790-39-PP, CEFH: 2020/07OCT/492), and was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki. All participants provided written informed consent prior to their inclusion in the study.

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SUPPORTING INFORMATION

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