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#### **Recommended Citation**

Kishen, A., Peters, O. A., Zehnder, M., Diogenes, A. R., & Nair, M. K. (2016). Advances in endodontics: Potential applications in clinical practice.. *Journal of Conservative Dentistry*, *19*(3), 199–206. DOI: 10.4103/0972-0707.181925 https://scholarlycommons.pacific.edu/dugoni-facarticles/361

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# Advances in endodontics: Potential applications in clinical practice

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#### Abstract

Contemporary endodontics has seen an unprecedented advance in technology and materials. This article aimed to review some of the challenges and advances in the following sections: (1) endodontic imaging, (2) root canal preparation, (3) root canal disinfection, (4) root canal filling, and (4) regenerative endodontic procedures (REPs). Jointly, these advances are aimed at improving the state of the art and science of root canal treatment.

Keywords: Canal preparation; disinfection; endodontic imaging; filling; regeneration

# **INTRODUCTION**

The past couple of decades have witnessed one of the most rapid and extensive technological evolutions in dentistry. This period has presented some remarkable developments of endodontic technologies. The current article is aimed to concisely review some of these advances pertinent to endodontic imaging, root canal preparation, root canal disinfection, root filling, and regenerative endodontic procedures (REPs).

# **ENDODONTIC IMAGING**

Analog and digital imaging modalities are available for use in diagnostic endodontic imaging. The National Council for Radiation Protection (NCRP) report #145 recommends the use of the fastest speed sensor with rectangular collimation to conform to the as low as reasonably achievable (ALARA) principle while capturing analog images. Analog imaging presents several disadvantages: Need for repeat exposure

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Date of submission : 22.01.2016 Review completed : 07.02.2016 Date of acceptance : 05.04.2016

Access this article online		
Quick Response Code:	Website: www.jcd.org.in	
	DOI: 10.4103/0972-0707.181925	

in suboptimal image capture situations, inability to enhance images interactively, wet processing issues, and difficulty in acquiring/transmitting images electronically, all of which have resulted in the adoption of digital technology. Digital capture systems include electronic sensors [digital radiography (DR)] such as a charge-coupled device (CCD) or a complementary metal oxide semiconductor (CMOS) while indirect systems use photostimulable phosphor (PSP) plates. This is known as computed radiography (CR). The advantages of digital imaging include significant dose reduction, relatively faster image acquisition, ability to enhance images, elimination of wet processing, easier transmission, and archival of images.

Currently hardwired and wireless sensors are available for use. DR offers the highest spatial and contrast resolution but the latitude is limited. CR offers wider latitude. Both have been shown to be as good as intraoral film or better for endodontic diagnoses. Most have active areas that are slightly smaller than film but more than sufficient for endodontic purposes. Advantages of CMOS over CCD include a lower manufacturing cost, need for a lesser amount of electrical energy for functioning, and comparable spatial/contrast resolution for diagnostic

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**How to cite this article:** Kishen A, Peters OA, Zehnder M, Diogenes AR, Nair MK. Advances in endodontics: Potential applications in clinical practice. J Conserv Dent 2016;19:199-206.

purposes. Presently available wireless sensors, including the newly introduced CMOS-APS sensors (Wifi Schick Elite sensor, Sirona Dental Inc., Long Island City, NY, USA) are less bulky and transmit signals *via* a thinner wire that enables wireless transmission and lasts for about 100 exposures.

PSP plates are wireless and activated by adding an impurity to the phosphor, thus rendering it sensitive to incident radiation. Charges are generated and stored in the form of a latent image following exposure. Exposing to white light would erase the plates and allow reusability. PSP plates require almost the same amount of exposure as an F-speed film with rectangular collimation. Plates are significantly less expensive than CCD or CMOS sensors. However, in endodontics instantaneous chairside acquisition of images with relatively high contrast and spatial resolution is required, which is best served by CMOS sensors.<sup>[1]</sup> Since multiple images are frequently needed, use of a sensor that requires the least amount of radiation to produce a high quality image is optimal in endodontics.

The processing of film carries several new recommendations as well. Transitioning to DR will help clinicians get into compliance fairly easily. For periapical and bitewing radiography, rectangular collimation should be used whenever possible because a round field beam used with a rectangular image receptor produces unnecessary radiation exposure to the patient. The human visual system is seriously limited in terms of the shades of gray it can view at any one point in time. Therefore, adjusting the display properties of the image optimizes visualization of the signal of interest. Images must be saved in a universal Digital Imaging and Communication in Medicine (DICOM) format for best fidelity and ease of transmission between imaging systems of different vendors. The compression scheme used does not result in loss of image data. Most newer systems permit a 16-bit depth (2<sup>16</sup> shades of gray) capture for an image. The file size is large and therefore, stored in a compressed format without the loss of diagnostic information (8-bit data).

The advent of cone beam computed tomography (CBCT) has resulted in widespread adoption of this technology image capture/processing. for three-dimensional Computed tomography greatly enhances diagnostic yield in certain situations where two-dimensional conventional radiographic studies have limitations. However, care should be exercised not to prescribe CBCTs for all endodontic procedures due to the fact that the radiation dose to the patient is significantly higher than those from conventional studies.<sup>[2]</sup>Apart from this, the presence of artifacts, noise, and lower spatial resolution as compared to conventional radiographs preclude the generation of useful images in several clinical scenarios. It is imperative that recommendations from the updated position paper on the use of CBCT in endodontics be carefully followed to keep doses to the minimum while maximizing diagnostic information from such cases. Several CBCT units are available with varying fields of view (FOV). Shortest scan times should be used with the smallest field of view and the smallest available voxel size without compromising on the signal to noise ratio but without a massive reduction in radiation as this would seriously degrade the signal quality. Voxel sizes range 76-500 microns but endodontic applications require voxel sizes of less than 200 microns for optimal spatial resolution. Those that employ smaller fields of view have smaller voxel dimensions. The existing literature supports the use of CBCT in clinical endodontics for selected diagnostic tasks, on a case-by-case basis, following a thorough clinical evaluation.

Few clinical studies have validated the use of CBCT in endodontics with the help of ground truth. Most are in vitro/ ex vivo studies, the results of which cannot be extrapolated to the clinical scenario. Care must be exercised in the use of CBCT in pediatric patients, in view of the fact that the American Academy of Oral and Maxillofacial Radiology (AAOMR) and American Association of Endodontists (AAE) support the Image Gently Campaign led by the Alliance for Radiation Safety in Pediatric Imaging to help minimize the radiation dose to children. Some of the potential applications of CBCT include diagnoses related to the following: Initial diagnosis where nonspecific signs and symptoms exist, dental anomalies and developmental disturbances, presence of anatomic variations, calcified canals, broken instruments, vertical root fractures, failure of prior treatment, nonsurgical and surgical retreatments, select cases of trauma, resorption (external and internal), and implant placement.<sup>[3,4]</sup>

# **ROOT CANAL PREPARATION**

All treatment steps in endodontics need to be assessed under the premise of antimicrobial effectiveness<sup>[5]</sup> and canal preparation is no exception. Root canal preparation serves to remove intracanal tissue (in vital cases) and necrotic material including microbial biofilms (in necrotic cases). In addition, an adequately shaped canal accepts irrigation solutions as well as interappointment medication and is ultimately filled optimally.

Engine-driven instrumentation continues to be used more frequently by endodontists compared to hand instruments.<sup>[6]</sup> At this point, several trends are observed in the marketplace:

- a. Application of more flexible alloys, which not only promises better canal negotiation but also extend the fatigue life.
- b. Practice of reciprocation motion and potentially reduction of the number of instruments used per patient.
- c. Introduction of instruments that are designed to

The following section will explore these trends and summarize expectations for the future. Table 1 provides an overview of current nickel-titanium rotary instruments.

Due to its specific metallurgical properties, nickel-titanium (NiTi) alloy can be manufactured so that it is, for example, at body temperature, predominantly either in austenitic or martensitic crystal configuration.<sup>[7]</sup> These two crystal configurations have distinctly different properties, with austenite being less flexible but allowing up to 7% recoverable elastic deformation range.<sup>[8]</sup> Conversely, martensite can be dead-soft and very flexible but only allows about 2% linear strain before nonrecoverable plastic deformation occurs.<sup>[9]</sup> With these differences in flexibility, distinct differences in fatigue resistance are observed: martensitic files have significantly extended lifespans.<sup>[9]</sup> Some martensitic instruments are designed to have deformations removed during sterilization cycles while reprocessing; however, regularly certain residual deformation still remains.<sup>[10]</sup> The development of specific heat treatment and production methods continues, which includes the fine tuning of the crystal conversion temperature so that instruments may for instance be very flexible when on the shelf while assuming a different shape and behaving more rigidly when placed in a root canal.

Currently, most practitioners use electric motors to power rotary instruments. These motors are also undergoing development. The ability to set a torque limit is common to most electric motors but many models currently allow reciprocating action. While this is not entirely new,<sup>[11]</sup> several NiTi instruments have been developed entirely for reciprocation motion with unequal angles of rotation. Reciprocation movement has been shown to be efficient and safe<sup>[12]</sup> In particular, fatigue lifespan of a file is extended with reciprocation design.<sup>[13]</sup> Irrigation efficiency in infected root canal systems may be facilitated by instrumentation via mechanical force<sup>[14]</sup> and perhaps a scraping action of instruments along the canal walls.<sup>[15]</sup> Toward this several techniques were initiated in the last few years, beginning with the so-called self-adjusting file.<sup>[16]</sup>

Clinical observations suggest that not only healing of apical periodontitis but also extended mechanical function of teeth is an important endodontic outcome.[17,18] Since it is well-understood that the major factor that increases fracture susceptibility in endodontically treated teeth is the removal of bulk dentin during access<sup>[19,20]</sup> and canal preparation,<sup>[21,22]</sup> strategies are being developed that retain more dentin,<sup>[23]</sup> specifically in the coronal root third<sup>[24,25]</sup> during shaping. One strategy to achieve this goal is to limit coronal flaring and perhaps the so-called maximum fluted diameter (MFD). A more radical change would occur if a completely noninstrumental technique without the use of any canal preparation was to be adopted. Such a technique was experimented years ago<sup>[26]</sup> requiring an airtight connection to the access cavity; currently, a noninstrumental canal disinfection system, based on ultrasonic activation, is being researched in vitro.<sup>[27]</sup>

In summary, most current instruments perform well when used judiciously; apical canal transportation, a measure

Name	Manufacturer	Description (tip diameter)	Production process
BioRace, BT Race, iRace	FKG-Brasseler	Triangular cross-section, multiple sequences, cont. rot. (10/.06-50/.06)	Grinding, electropolishing
EdgeFile X1, 3, 5, 7	EdgeEndo	Parabolic cross-section, cont. rot., (17/.04-40/.06)	Grinding, heat treatment
Hyflex/Hyflex CM	Coltene	Triangular cross-section, cont. rot., martensitic alloy (15/.04-40/.06)	Grinding (electrical discharge machining)
K3XF	Kerr Sybron	Complex cross-section, R-phase alloy, cont. rot. (15/.04-60/.06)	Grinding, heat treatment
OneShape	MicroMega	Two s-shapes cross-sections, cont. rot. (25/.06)	Grinding, heat treatment
ProTaper gold	Dentsply Tulsa Dental	Variable tapers, partly martensitic alloy, cont. rot. (17-50, various apical tapers)	Grinding, heat treatment
ProTaper next	Dentsply Tulsa Dental	Variable tapers, rectangular off-centered cross-section, cont. rot. (17/.04-50/.06)	Grinding, heat treatment, electropolishing
Reciproc	VDW	Two flutes in s-shaped cross-section, Reciprocation with unequal angles (25, 40, 50)	Grinding, heat treatment
SAF	Redent Nova Henry Schein	2 sizes, hollow-tube mesh, in-out-translational movement	Laser cutting, heat treatment
TF Adaptive	Kerr Sybron	Multiple sizes, special motor with various rotation modes	Twisting, heat treatment
TRUShape	Dentsply Tulsa Dental	Triangular cross-section S-shaped, cont. rot. (20-40, conforming taper)	Grinding, heat treatment, form-pressing
Typhoon	DS Dental	Triangular cross-section, martensitic alloy, cont. rot. (20/.04-35/.06)	Grinding
Wave0ne	Dentsply Maillefer	Reciprocation with unequal angles, currently 3 tip sizes (21, 25, 40, various apical tapers)	Grinding, electropolishing
Vortex Blue	Dentsply Tulsa Dental	Triangular cross-section, partly martensitic alloy cont. rot. (15/.04-50/.06)	Grinding, heat treatment

 Table 1: Nickel-titanium root canal preparation instruments introduced after 2010

cont. rot. = Continuous rotation

of shaping quality, is typically under 150  $\mu$ m.<sup>[28]</sup> Flexibility and resistance to fatigue of the instruments are increasing. Current and future developments of instruments and strategies are aimed to provide antibiofilm effects and remove less radicular dentin structure. As shaping alone is not sufficient to reduce microbial loads, adequate irrigation strategies will continue to complement canal preparation.<sup>[29]</sup>

# **ROOT CANAL DISINFECTION**

Complexities of the root canal systems, in addition to the structure and composition of the dentin, are key challenges for effective disinfection in endodontics. Topical antimicrobial such as sodium hypochlorite is commonly used in root canal treatment to combat microbial biofilms. The inability of antimicrobials to eliminate biofilm bacteria in the anatomical complexities and uninstrumented portions of the root canal would compromise their efficacy in root canal treatment. Irrigation dynamics deals with how irrigants flow, penetrate, and exchange within the root canal space and the forces produced by them. Unfortunately, the widely used syringe-based irrigation displayed a passive flow of irrigant at the apical region, 1-3 mm beyond the exit of the needle. The syringebased method also failed to generate optimum levels of shear stresses on the canal wall, which is significant for disinfecting root canal biofilms. Thus, steps taken to improve the delivery of irrigant (irrigation dynamics) within the root canal system are crucial to achieve the maximum efficacy out of the antimicrobials. The current advances in endodontic disinfection are aimed toward:

- a. Improving the fluid dynamics during root canal irrigation improving bubble dynamics and activating intensified cavitational bubbles are some of the mechanisms by which fluid dynamics can be improved.
- b. Developing newer antimicrobials, which demonstrate potent antibiofilm effect over sodium hypochlorite.<sup>[30]</sup>

#### **Antibacterial nanoparticles**

Nanoparticles (NPs) are microscopic particles with one or more dimensions in the range of 1-100 nm. It is established that NPs have properties that are very unique from their bulk counterparts. Antibacterial NP has been found to have a broad spectrum of antimicrobial activity and far lower propensity to induce microbial resistance. The electrostatic interaction between positively charged NPs and negatively charged bacterial cells, and the accumulation of large number of NPs on the bacterial cell membrane have been associated with the leading to the loss of membrane permeability and rapid loss of membrane function.<sup>[30]</sup> The ability of some of the tested NPs to rapidly eliminate biofilm bacteria needs further improvement. However, when sealers are loaded with NP, they displayed a superior ability to diffuse the antibacterial component deep into the dentin.<sup>[31]</sup> Studies have stressed their role as an intracanal medicament than an irrigant, and to improve the antimicrobial effectiveness of root canal sealers.<sup>[32]</sup> Currently, functionalized NPs are being developed to eliminate bacteria more specifically without damaging the host cells (targeted antibacterial efficacy) and to repair previously infected dentin matrix.<sup>[33,34]</sup>

#### Antimicrobial photodynamic therapy

Antimicrobial photodynamic therapy (APDT) is a two-step procedure that involves the application of a photosensitizer (PS) (step-1), followed by light illumination (step 2) of the sensitized tissue, which would generate a toxic photochemistry on the target cell, leading to microbial killing. Currently, APDT is considered not an alternative but a possible supplement to the existing protocols for root canal disinfection.<sup>[30]</sup> In an approach to adapt and improve the antimicrobial efficacy of APDT in endodontics, recent research has developed novel formulations of photosensitizers that displayed effective penetration into dentinal tubules, anatomical complexities, and antibiofilm properties. Well-designed clinical studies are currently warranted to examine the prospects for APDT in root canal disinfection.<sup>[35,36]</sup>

#### Photon-induced photoacoustic streaming

Photon-induced photoacoustic streaming (PIPS) is based on the direct shock wave generated by a erbium:YAG (Er:YAG) laser (Fidelis AT; Fotona, Ljubljana, Slovenia) in a liquid irrigant. The laser system is equipped with a fiberoptic delivery tip and subablative parameters to produce the desired effect. When activated in a limited volume of fluid, the high absorption of Er:YAG wavelength combined with the high peak power derived from the short pulse duration resulted in an enhanced bubble dynamics, which improved the irrigant flow dynamics within the root canal. The current literature presents conflicting findings on this technology.<sup>[37-39]</sup> This demands further evaluation and modifications of this technology to optimize therapeutic efficacy through the root canal system.<sup>[40]</sup>

#### **Gentlewave irrigation**

Gentlewave (GW) (Sonendo, Laguna Hills, CA, USA) has been developed and tested for root canal irrigation. It delivers sodium hypochlorite into the root canal under pressure through a specialized handpiece, which is activated by a broad spectrum of acoustic waves. At the same time, suction removes the outflowing fluid through the handpiece. A silicon ring surrounding the extremity of the handpiece creates a tight seal with the artificially created flat tooth surface. This establishes a vented and closed-loop fluid flow within the root canal.<sup>[27]</sup> This system is expected to enhance irrigation dynamics in minimally enlarged root canals. Studies are currently being performed to assess the ability of the GW system to disinfect the root canal biofilms.<sup>[37]</sup> In summary, many advanced antimicrobial strategies are being tested and developed to enhance antibiofilm efficacy within the root canal system. These techniques are focused toward potent antibiofilm methods and optimized irrigant delivery systems to achieve essential goals in root canal treatment. Further clinical research is required in this area.

#### **ADVANCES IN ROOT FILLING**

To complete a root canal treatment in a mature tooth, the root canal system is filled with synthetic materials. A predictable alternative to this technique is currently elusive. It may be possible in the future to attract pulp-like tissue into the cleaned and shaped root canals.<sup>[41]</sup> However, the translation of tissue engineering concepts to everyday clinics has not yet been made and thus, the current focus to improve the conventional approach to fill the root canals will still remain.

Primarily, the root-filling is expected to provide a hermetic seal against microorganisms, be tissue-friendly, easy to apply, monitor, and retrieve in case of treatment failure. These requirements are not always met by current filling materials.<sup>[42]</sup> The core of the problem with current materials is that a so-called hermetic seal is not easy to achieve.

Why is a hermetic seal difficult to achieve in root canals? Any material that is used to fill the small anatomical intricacies of a tooth needs to be applied in a plastic state. Later, this material should be dimensionally stable. With the synthetic materials used in dentistry, this means that some form of physical or chemical reaction takes place between the application of a filling material and its final state. In the context of filling root canals, we encounter the problem that the configuration factor (C-factor), which is the ratio between bonded to nonbonded area of a filling material, is extremely high in the root canals.<sup>[43,44]</sup> This means that the volume shrinkage is more detrimental to the cohesiveness of the tooth and filling in this environment than in the crown of the tooth. When a material alters its state, it usually changes its dimensions. For root-filling materials in particular, dimensional changes should be kept minimal. While most current sealers, especially those based on an epoxy resin or silicone, are dimensionally stable<sup>[45]</sup> the core material is not. In current root-filling techniques, guttapercha (essentially polyisoprene with a high zinc oxide filler content) is used as a core material. It is heated to become plastic, and applied in conjunction with a sealer. However, it was well-recognized that thermoplasticized gutta-percha shrinks upon cooling.<sup>[46]</sup>

*Some newer concepts:* Two related concepts have evolved over the recent years that might improve and simplify root-filling procedures. The first approach is to use a calcium silicate cement-based sealer.<sup>[47,48]</sup> These sealers

are initially flowable and express bioactive properties, i.e., they promote Ca/P precipitation in a wet environment. As the root canal system is inherently wet,<sup>[49]</sup> the use of bioactive filling materials is logical.<sup>[48]</sup> The interface that forms between sealer and root canal wall is calcium phosphate and thus, mimics nature. Since calcium-silicate cements set hard, a core material is still necessary, which remains to be gutta-percha. Consequently, root-fillings with calcium-silicate cements still have two interfaces:

- a. Between the sealer and the canal wall, and
- b. Between the sealer and the gutta-percha.<sup>[50]</sup>

Hence, calcium silicate sealers *per se* do not conclusively solve the root-filling conundrum.

In a recent approach, bioactive particles were embedded in the matrix (polycaprolactone) of the core filling material.<sup>[51]</sup> This matrix material was thermoplasticized and used as the sole material to fill root canals, thus reducing the interface between filling and tooth to one, with rather promising results in vitro. However, polycaprolactone appears not to be an ideal material for root-fillings, as it is biodegradable.<sup>[52]</sup> A later approach used nanometric bioactive glass particles of the 45S5 type embedded in the gutta-percha matrix.<sup>[53]</sup> In contrast to conventional gutta-percha, this material showed immediate sealing properties when applied in heated form. A premarket radiopaque material was later introduced and tested for its self-adhesiveness to the root dentin<sup>[54]</sup> and tissue compatibility.<sup>[55]</sup> The initial *in vitro* results were promising, yet the material has to be scrutinized clinically before final recommendation.

Complex application schemes<sup>[56]</sup> and uncontrolled/extended thermal shrinkage<sup>[57,58]</sup> are some of the challenges in current root-filling. Newer nanomaterial-based approaches are showing promise for the future.

#### **REGENERATIVE ENDODONTICS**

The treatment of immature teeth with pulpal necrosis represents a major clinical challenge. The untoward advent of pulpal necrosis arrests the developmental process in immature teeth.<sup>[59]</sup> The challenges related to treating these cases far exceed the technical challenges of debriding and obturating a large root canal space with thin dentinal walls, and lacking an apical constriction. These teeth have been traditionally treated with apexification procedures. Although these procedures are quite successful in arresting the infectious process and resolving apical periodontitis, they fail to promote continued root development and normal physiological pulpal responses. Thus, immature teeth remain with thin fragile dentinal walls becoming susceptible to fractures and lower survival. Further, implants are contraindicated in patients undergoing cranioskeletal development. Thus, there has been an unmet need to provide adequate treatment to patients with immature teeth with pulpal necrosis.

The field of regenerative endodontics emerged in early 2000s with the publication of two remarkable case reports.<sup>[60,61]</sup> Since then, there have been more than 200 published cases demonstrating that these procedures allow unprecedented results.<sup>[59,62,63]</sup> These include:

- 1. Resolution of apical periodontitis and signs and symptoms of pulpal inflammation;
- 2. Radiographic evidence of continued root development and apical narrowing; and
- 3. Restoration of vitality responses.

Importantly, these published cases demonstrate that REPs address the unmet need of promoting normal physiological development and responses in immature teeth diagnosed with pulpal necrosis.

In most REPs, clinicians rely on creating bleeding from the apical region that passively fills the canal space and forms a blood clot. However, it was not until 2011 that a clinical study demonstrated that the influx of apical blood into disinfected root canals allowed a significant transfer of stem cells into the root canal system. This was a very important pivoting moment in this young field of regenerative endodontics since it established that these procedures were in fact, stem cell-based procedures. The realization that stem cells were present in root canals during these procedures propelled researchers to investigate the effect of various steps usually employed on these procedures on stem cell fate.

The balance between adequate disinfection and stem cell survival, proliferation, and differentiation represents an important first barrier to be overcome. The resolution of infection and the disease process remains the primary goal of any endodontic procedure. However, it has become obvious that the philosophy of disinfecting the root canal at all costs typically advocated in traditional root canal therapy had to be modified to a "biocompatible disinfection" strategy. For example, sodium hypochlorite remains the most used disinfectant in endodontics.<sup>[64]</sup> However, its use at full concentration of 6% denatures crucial growth factors in the dentin<sup>[65]</sup> and results in residual detrimental effects greatly affecting stem cell survival and differentiation potential.<sup>[66-68]</sup> These effects can be largely avoided with the use of the concentration of 1.5% followed by 17% EDTA.<sup>[68,69]</sup> Another example is the long-lasting detrimental effects of using high concentrations of antibiotic pastes (approximately 1 g/mL) as intracanal medicament on stem cells. At this concentration, triple antibiotic paste (minocycline, metronidazole, and ciprofloxacin) have longlasting effects on stem cell survival through both direct and indirect mechanisms.<sup>[70,71]</sup> This undesirable carryover effect can be greatly avoided by the use calcium hydroxide

as intracanal medicament<sup>[70,71]</sup> or the use of these pastes in lower concentrations (<1 mg/mL) while maintaining their desirable antibacterial effect.<sup>[72,73]</sup> Therefore, there has been significant advancement in understanding how to adapt currently used disinfection protocols to the reality of stem cell-based therapies.

Apart from biocompatible disinfection, many other frontiers in regenerative endodontic research are being currently investigated. These involves tissue engineering strategies that include the evaluation of suitable scaffolds, growth factors, and harvested stem cells to be used in pulpal regeneration.<sup>[74]</sup> Importantly, many of the advances from translational research have been transferred to clinical practice such as the use of platelet-rich plasma,<sup>[75,76]</sup> platelet fibrin,<sup>[77]</sup> and a gelatin hydrogel<sup>[78]</sup> as scaffolds in patients. In addition, a groundbreaking clinical trial is currently in process in Japan. This trial involves harvesting stem cells from a donor site followed by *ex vivo* expansion, sorting, and autotransplantation into a recipient tooth to promote the regeneration of the once lost functional pulp–dentin complex.<sup>[79]</sup> These elegant studies highlight the current status and sophistication of REPs.

In summary, significant advances in regenerative endodontics allow better understanding of a multitude of factors that govern stem cell-mediated regeneration and repair of the damaged pulp–dentin complex. Translational research is proving to be crucial in making these procedures more predictable while pushing the boundaries of future procedures that are likely to involve the direct clinical manipulation of scaffolds, growth factors, and stem cells.

#### **Financial support and sponsorship** Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

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