Nanomaterials Application in Endodontics

Subjects: Nanoscience & Nanotechnology
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The medical procedures in endodontics are time-consuming and mostly require several visits to be able to achieve the proper result. In this field of dentistry, there are still major issues about the removal of the mostly bacterial infection from the dental root canals. It has been confirmed that nanoparticles are much more efficient than traditional materials and appear to have superior properties when it comes to surface chemistry and bonding. Their unique antibacterial properties are also promising features in every medical procedure, especially in endodontics. High versatility of use of nanomaterials makes them a powerful tool in dental clinics, in a plethora of endodontic procedures, including pulp regeneration, drug delivery, root repair, disinfection, obturation and canal filling.

Keywords: nanomaterials ; endodontics ; dentistry

1. Introduction

One of the branches of dentistry that deals with the morphology and physiology of the endodontium is endodontics. It combines such aspects of this field as etiology, pathology, epidemiology, prophylaxis and, above all, treatment of endodontic and periapical diseases. Depending on the complexity of the case, the treatment process may be carried out at one or more visits. Due to the difficulty of maintaining the sterility of the operator's work area, nanomaterials are increasingly used. Thanks to the expanding variety of nanoparticles, such as bioactive glass, zirconia, chitosan, hydroxyapatite, silver particles, zinc oxide, the properties of materials used in dentistry, such as durability, tissue regeneration and bactericidal properties, can be improved.

2. Classification of Nanomaterials, Materials Modification

Generally, nanoparticles can be divided into naturally occurring and artificial due to their composition. The subgroup of naturally occurring nanoparticles divides into inorganic or organic. As for the shape, nanoparticles can be divided into spherical, tubular, rod-shaped and plate-shaped particles. In addition, functionalized nanoparticles can also be distinguished. They have an inner part-core, that is built of one material with different molecules on its outer surface or enclosed in it. Depending on application, particles in nanomaterials can be modified by using, among many things, drugs or peptides [1]. The mechanism of functionalization is focused on the functioning of linker molecules in which each linker molecule has at both its ends a reactive group that binds different molecules—such as biocompatible materials (dextran), antibodies, fluorophores and others—to the core of the nanoparticle. On the other hand, the core nanoparticle can be used as a surface for assembling particles from inorganic or organic materials [2].

Another classification method for nanomaterials is their division by dimensions, as illustrated in **Figure 1**; materials can be produced in a nanoscale in either zero (e.g., fullerenes), one (thin surface coatings), two (e.g., graphene), or three dimensions (composite nanomaterials).

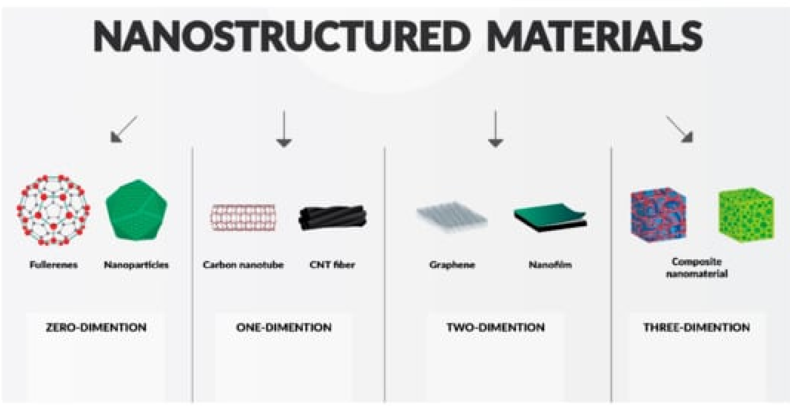


Figure 1. Graphical representation of the nanostructured materials dimensional division.

2.1. Quantum Influence on Nanomaterials

2.1.1. Quantum Confinement Effects

When it comes to nanomaterials, it is important to underline that quantum effects are not dominant in macro- and micro-sized materials, even though they are present in the nano scale. Quantum effects may affect the electrical, magnetic and optical behavior of materials.

Roduner et al. [3] point out why nanomaterials are different from their larger-in-scale counterparts. One of the many differences is the catalysis processes on their surfaces. It changes the chemical, physical, as well as electronic properties. Quantum confinement effects describe electrons in terms of electron energy band gaps, conduction bands, valence bands, potential wells and energy levels [4]. It is present when a particle is too small to be comparable with electron wavelength. This is a general condition that is strictly limited by specific material properties, especially Bohr radius [5]. The density of states (DOS) can be explained as a model of ‘particle in a box’, where the size of the particle is directly proportional to the size of the box [6].

2.1.2. Surface Effects

Nano-sized materials have novel characteristics that are absent in the behavior of molecules forming a bulk [7][8][9]. When the number of molecules in the nano-scale is reduced, the materials usually reach a point at which the whole substance starts to behave in a way which is more characteristic for molecules than for a bulk matter. To understand the thermophysical properties of nanomaterials better, theoretical research is required [10][11][12][13][14]. The general rule is that mechanical and thermodynamic parameters are reduced with decreasing size of particles. Among many features, it applies to Young’s modulus [15], mass density [16], cohesive energy [17][18] and melting point [19][20][21]. Macroscopic thermodynamics does not apply to nanomaterials because of the differences in the binding energy that affects them. As L. D. Gelb et al. [22] confirmed that phase transition is less visible in nano-phase than in macro-phase. Instead of using the concept of ‘phase’, it can be more correct to speak of ‘different structural isomers’ that coexist over a range of temperatures [23].

2.2. Chitosan Nanoparticles

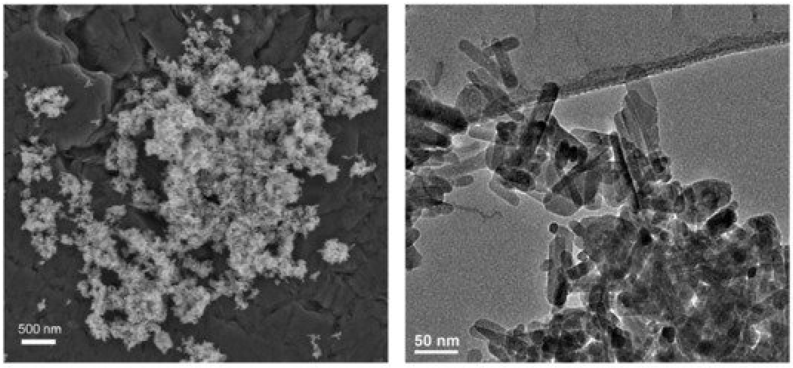
Chitosan is an organic chemical compound from the group of polysaccharides. This non-toxic biodegradable substance is obtained from the deacetylation of chitin in alkaline media. Sources of this homopolysaccharide are the exoskeletons of arthropods, mollusks and insects. Chitosan is a polysaccharide containing deacetylated units and acylated units. These unit are, respectively: D-gucosamine and N-acetyl-D-glucosamine. Due to its availability in many forms such as hydrogels, capsules or scaffoldings, it of interest as a material for biomedicine [24]. In general medicine, it is useful as a bandage mimics the native extracellular matrix, ensuring the appropriate microenvironment of the wound, thus accelerating its healing. In endodontics, chitosan can be used mainly due to its antibacterial properties [25], especially against *E.faecalis* strain [26][27].

Regarding its unique chemical structure, it has many applications (alike only or as an alternative combine with other natural polymers), such as medical use, cosmetic use, also bio-printing, agricultural and horticultural use [28]. In biomedical engineering chitosan nanoparticles are being used in view of physicochemical properties such as, particularity, biocompatibility and sensitivity [29].

2.3. Hydroxyapatite (HAp)

The naturally occurring mineral form of calcium apatite is hydroxyapatite (HAp). It is mainly obtained from mineral tissue [30]. Hydroxyapatite is highly biocompatible due to the fact that HAp is one of the main constituents of dentin. In addition, it can also quickly osseointegrate with the supporting connective tissue (bone tissue). HAp is used in a variety of forms, equally as composites, coatings [31] and powders [32] for dental fillings in view of these advantages.

The high bioactivity of nanohydroxyapatite results from its similarity to bone apatite as well as its strong ion exchange affinity. In addition, its biological properties are determined by the size and morphology of molecules, the type of ionic impurities in the crystal lattice and the Ca/P molar ratio [33][34], resulting in its hexagonal system crystallization [35]. In addition, its biological properties are determined by the size and morphology of the molecules (**Figure 2**).



(A) (B)

Figure 2. (**A**) SEM image of the nHAp; (**B**) TEM image for nHAp.

2.4. Bioactive Glass

In 1960, Hench et al. developed bioactive glass which consisted of strictly defined proportions: sodium oxide, calcium oxide, phosphorus pentoxide and silicon dioxide. This material is widely used in tooth repair due to its ability to bind to bones [36]. Additionally, bioactive glass has excellent regenerative and antimicrobial properties. Its structure allows new bone tissue to be regrown directly onto it, as is visualized in **Figure 3**. The process of bone tissue regrowth is possible due to the similar chemical composition of bioactive glass, human bone and dentin.

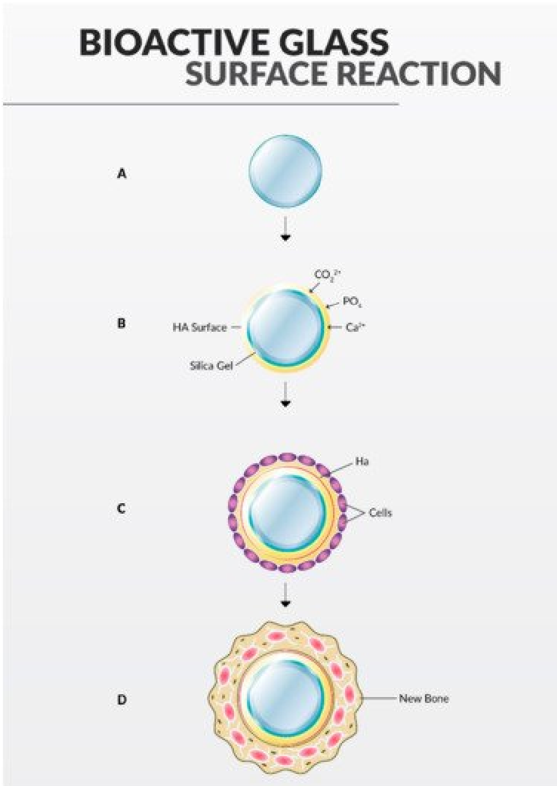


Figure 3. Formation of new bone tissue on bioactive glass. (**A**)—bioactive glass. (**B**)—adhesion of ions to the sillica surface, which results in a formation of bone-like HA. (**C**)—osteogenic cells cover the surface of the hydroxyapatite and create a coated bioactive glass. (**D**)—crystallization leads to the formation of a new bone tissue.

2.5. Zirconia (Zr)

Zirconia (Zr) is a stabilized regular modification of zirconium oxide. This material is characterized by: high wear resistance, good optical properties and low reactivity. As a result of its properties, it is used in implantology, as well as in dental restorations [37][38].

Endodontic treatment causes the reduction of the tooth's mineral tissue (its loss) and consequently, weakening of the tooth. The reduced amount of tooth tissue makes its reconstruction difficult. Core buildups are used to retain core materials that are predictably delivered with state-of-the-art resin composites [39][40]. Therefore, the core material (its mechanical and physical properties) is important in the endodontic restoration of the tooth. To strengthen the structure of the weakened tooth, nanoparticle-sized fillers for composites are used. The great biocompatibility and mechanical properties of zirconium nanoparticles make it enriched with composite resins.

2.6. Nanosilver

The antimicrobial, anti-inflammatory, thermal and optical properties of silver made it popular in medicine [41]. In dentistry, silver is mainly used for its antimicrobial properties. The rate of silver ions release determines its unique antibacterial properties. Silver is considered fairly inert even though it exhibits metallic properties and it becomes highly reactive due to the fact that it is ionized with moisture. The antibacterial properties of silver are related to the fact that it binds to tissue proteins of the cell wall, thus changing its structure and, consequently, destroying the bacterial cell [42].

2.7. Zinc Oxide (ZnO)

Resin-based root canal sealants can be enriched with nanoparticles of, i.e., ZnO. Enrichment of sealants with zinc oxide nanoparticles improves antimicrobial properties through better diffusion of root canal sealants. Research has shown that endodontic microorganisms are closely related to gutta-percha (a common material for filling root canals) [43][44]. Often the cause of infection in the root canal is the adhesion of bacteria and the formation of biofilms on the gutta-percha. In such cases, increased effectiveness of root canal disinfection could be possible due to the long-term antimicrobial properties of root canal sealants. In most cases of the sealants used, a decrease in the antimicrobial properties is observed immediately after binding. However, those commonly used retain its antimicrobial properties for a maximum of 1 week after binding [45][46]. A high percentage of *E. faecalis* bacteria reduced the adhesion to the dentine by treating the dentine of the root with ZnO nanoparticles, ZnO/CS mixture, ZnO of the CS layer or NP CS [47]. Magnesium oxide and calcium oxide suspensions have a bactericidal effect on both gram: positive and negative bacteria. On the other hand, zinc oxide suspension has a stronger antibacterial effect against Gram-positive than Gram-negative bacteria, and also has a bacteriostatic effect [48].

2.8. Exosomes

Various MSCs participate in the process of pulp formation, such as dental pulp stem cells (DPSC), human exfoliated deciduous tooth stem cells (SHED), apical papilla stem cells (SCAP), and dental alveolar progenitor cells (DFPC) [49]. Zhou et al. [50] proved that microballoons from dental pulp stem cells (DPSCs) can be used in regenerative endodontic therapy due to their pro-angiogenic effect.

2.9. Graphene

Graphene has many properties that can be used in dentistry, including antibacterial activity, potential use of graphene in tissue engineering, dental implants, in the field of endodontics, periodontics and conservative dentistry.

Graphene nanoplate exhibits antimicrobial properties due to the sharp edges of GNP flakes piercing the soft cell wall of the bacteria, resulting in their trapping and shrinkage [51]. These results suggest that *Streptococcus mutans* (*S. mutans*), which is responsible for human caries, can be combated in this way.

2.10. Nanopolymers

Quaternary polyethylene ammonium (QPEI) is a nanopolymer that exhibits insolubility, biocompatibility and chemical stability in contrast to other materials used in chemo-mechanical root canal disinfection such as calcium hydroxide materials [52]. The studies conducted by Abramovitz et al. show, that nanopolymers of quaternary ammonium polyethyleneimine (QPEI) have a long-lasting antibacterial activity against both Gram-negative and Gram-positive bacteria [53].

When added to the epoxy resin sealant, this material reduces the viability of *E. faecalis* in dentinal tubules. As a consequence, endodontic treatment is more effective and thus the likelihood of complications caused by bacteria affected by QPEI is reduced.

3. Clinical Applications

3.1. Sealers

The crucial functions of an endodontic sealer are to make the seal impervious. This can be provided by filling in the minor distortions and irregularities that may occur between the root canal wall and the stem filling material. In addition, if the microorganisms remain in the lateral canals or tubules, the sealant then fulfills the microbiological control. Studies have shown that bacteria that occur in root canals survived at 40–60%, despite the use of different concentrations of NaOCL in the chemo-mechanical method of root canal cleaning [54]. Most sealants show mild antimicrobial properties. This is a consequence of the release of eugenol, paraformaldehyde or zinc oxide. However, these properties gradually diminish as the sealant sets [55]. The quality of the root canal filling is greatly influenced by the thickness of the endodontic sealant layer. Only a thin layer should be evenly applied to the canal walls because it shrinks during setting and leaves unwanted voids. Moreover, these sealers gradually dissolve [56].

Silver (Ag), calcium oxide (CaO), copper oxide (CuO), zinc oxide (ZnO), chitosan (CS), magnesium oxide (MgO) and QAPEI nanoparticles have been investigated as potential antimicrobial agents and to improve physicochemical and biological properties.

Epoxy resins are among the materials that are the most popular with clinicians because of their high pressure resistance, good marginal adhesion and minimal solubility in tissue fluids. They also exhibit antimicrobial activity and can form chemical bonding with dentinal collagen [57]. Moreover, they are characterized by a long working time and good availability. Significant disadvantages of these materials are the difficulty of removing them from the root canal system and some degree of cytotoxicity, which may vary [58].

Barros et al. [59] proved by conducting the test that, by adding 1% or 2% nanoparticles of QPEI, it influences the antimicrobial effect of sealants (in particular, with oral cavity bacteria). Adding a nanoparticle to the sealant does not significantly affect compressive strength, dimensional change, solubility, flowability, apparent porosity or change of setting time. QPEI has a positive charge and is hydrophobic—after its incorporation, sealers become hydrophilic. Therefore, it is possible to use it as an antibacterial biomaterial. and QPEI nanoparticles enhanced antibacterial effectiveness against *E. faecalis* strains. After seven days, no significant changes in mechanical and physicochemical properties were noticed.

Beyth et al. [60] observed that antibacterial effects against *S. mutans* and *E. faecalis* are obtained mainly by adsorption and penetration through the bacterial cell wall. In the next stage, it interacts with proteins and the fat layer in the cell membrane. Subsequently, the exchange of essential ions is blocked, the cell membrane is destabilized and, consequently, cell death occurs [61]. Physicochemical and mechanical tests carried out by Barros et al. showed that it is possible to increase the penetration capacity of the sealant into the root canals by adding QUPEI nanoparticles to it. The type of sealant and the type of cell determine the proliferation and differentiation of bone cells without increasing the cytotoxicity of the sealant. Scientists have demonstrated this by adding 2% of QPEI molecules to AH Plus and PCS.

3.2. Obturating Materials

Removal of infected tissues from root canal systems, their disinfection and tight filling with proper protection of the tooth crown are the standards of the modern approach to endodontic treatment. After removing the content of the tooth cavity and shaping the canal properly, the root canal should be hermetically filled in three dimensions to prevent being recolonized by microorganisms. Moreover, it provides the isolation of any pathogens from the saliva that are responsible for percolation from the coronal region, the gingival sulcus or periodontal pockets. Only hermetic filling from the coronal orifice to the physiological foramen protects tissues from disease processes, and in the case of existing inflammations, it determines their healing. Obturation is a critical moment and is often the reason why endodontic treatment fails. Several techniques and materials have been developed to provide the cohesive and adhesive interaction of filling materials with the walls of the root canal system. The properties required of perfect filling materials used in endodontic treatment are biocompatiblility with the tissue, stimulation, or at least support of the regeneration of damaged cells, easy adaptation to and removal from the canals, antimicrobial activity, adherence to the canal walls and dimensional stability over time, water insolubility, good handling and flow characteristics, radiopacity, imperviousness and non-porosity, both local and systemic nontoxicity, lack of tooth discoloration, reinforcement, support and strengthening of the root structure as well as affordability and a long shelf-life [62].

Currently, despite the advances in materials engineering and molecular biology, no material has been developed that would meet all of these requirements. A wide range of them have been presented over the past decade for root canal filling, from gold and silver cones, gutta-percha, Resilon, calcium phosphate, MTA and various types of sealers.

The basic concept of three-dimensional root canal filling involves the use of two materials at the same time—the main one acting as a core with solid or semi-solid consistency, and the other with a semi-solid consistency acting as a sealer, filling the space between the dental wall and the obturating core interface and flowing into multiple canals, fins, deltas, and lateral canals. The most commonly used material for the main filling is gutta-percha. It is used both in cold filling methods including a single gutta-percha cone and lateral compaction, or warm filling methods such as warm vertical or lateral compaction, thermoplastic injection technique, root canal filling with a gutta-percha coated carrier, continuous wave compaction technique. Research shows that gutta-percha alone, even thermoplasticized, does not provide adequate three-dimensional filling and should be used with sealers [63].

Gutta-percha is a thermoplastic polymer of natural origin. Chemically it is trans-1,4-polyisoprene and can exist in different crystal forms—alpha and beta—as well as in the isomeric-amorphous gamma phase. In dentistry, the most commonly used form is the beta configuration in the form of a gutta-percha cone, which is stable and flexible at room temperature and is less adhesive and flowable when heated [64].

Regarding the lack of true adhesion of GP and consequently microleakage, root canal reinfection, and not enough completed mechanical properties, attempts were made to use additives to improve these capacities [65]. Researchers have investigated the medical activity of gutta-percha cones containing different substances including calcium hydroxide, bioceramic, resin, iodoform, zinc oxide, nonthermal plasma-argon, and oxygen plasma chlorhexidine, and cetylpyridinium chloride alone or used in combination [64][66].

Scientists have also explored nanodiamonds (NDs) and nanosilver particles as an alternative modification to obtain optimum sealing and therapeutic effects [67]. Gutta-percha coated with nanosilver particles (AgNPs) exhibited antiseptic properties. After modification, this combination has shown antibacterial activity against *E.faecalis*, *Staphylococcus aureus (S. aureus)*, *Candida albicans (C. albicans)* and *Escherichia coli (E. coli)*. In in vitro studies on mouse fibroblasts, Shantiaee et al. [68] indicated that this material is biocompatible and has cytotoxicity like standard gutta-percha. In their investigation, it achieved the lowest level of cytotoxicity among the tested materials after one week.

3.3. Nano-Size Related Drug Delivery Applications in Endodontics

In recent years, nanotechnology has been developing rapidly in various fields of medicine. The development of nanotechnology is also taking place in medicine, including dentistry. Thanks to the variety of liposomes, micelles, polymer-based nanoparticles (NPs), nano-emulsions, nanogels, inorganic NPs, the nano-drug delivery system can have so many applications [69]. The small size of the drugs allows for their more precise application, which is also associated with their lower cytotoxicity. Drug delivery systems can be divided into nano drugs as their own carriers, nano drugs with nano carriers, nano drugs with other carriers or drugs with nanocarriers [70]. Nanofibers are one of the examples of drug carriers in endodontics. Thanks to their biocompatibility and resemblance to lost tissues and bactericidal properties, they can be an alternative to commonly used agents. In the case of pulp revascularization, various forms of nanoparticles (nanotubes, nanofibers, matrices) are used. The latter are classified into those compounded with polyacids (lactic, glycolic and caprolactone).

3.4. Root Repair Materials

Nanotechnology has also revolutionized the way of producing root repair materials. Nanometric particles significantly improved the physical parameters of the material, positively affecting treatment results. Obtaining nanoscale particles enables the design of materials with precise and ultra-fine architecture, which significantly improves the filling properties of the material. Nanoparticles are able to more accurately fit into the complex shape of the tooth canal. Improving the adhesion and tightness of the material used increases the percentage of successful root canal treatment [71][72].

Root repair materials, due to their biocompatibility, bioactivity and a number of physical features, are used in a variety of dental procedures, for example in endodontics. Mineral trioxide aggregate (MTA) is the first successful material used in treatment. You can use it in many situations in endodontics, such as perforations, root canal treatment, surgical treatment of apex resection. It can also be used for canal filling [73].

As described in a study by Mohammed S Alenazy et al. [74], the material of choice for backfilling is MTA, but it has long processing and setting times. To overcome these negative properties, studies used MTA in nanomodified particles for improved physicochemical properties. They discovered that when MTA was used in the form of nanoparticles, the surface area was increased for the powder in contact with tooth tissues, which makes setting time shorter and growth the hardness of the material. This change apparently helped MTA solidify faster. Unfortunately, the use of nanomaterials was associated with the deterioration in the required hardness after full setting. Additionally, despite its great recognition, MTA is not without its disadvantages—mainly in terms of biocompatibility, strength, setting time, and biological and physical properties. This limitation seems to be another challenge for nanomaterials in root repair materials.

3.5. Nanoparticle-Based Disinfection in Endodontics

One of the most important elements of root canal treatment is cana disinfection by irrigation. Irrigation allows us to remove the infected tissues inaccessible to mechanical treatment alone. Theoretically, the irrigation fluid is able to reach all areas of the canals, removing pathological tissues from them, without damaging healthy tooth tissues. In modern times, using nanoparticles to irrigate the teeth canals has attracted attention. Silver nanoparticles are one of the materials used for this purpose. They have antibacterial and antifungal properties [75]. However, they are also likely to have inflammatory, oxidative, genomic and cytotoxic effects [76]. Researchers are looking for ways to use silver nanoparticles safely. An example is the use of antimicrobial photodynamic therapy based on nanoparticles [77]. In the work of Pagonis, the effect of polylactoglycolic acid (PLGA) nanoparticles together with the use of light was investigated (in vitro study). The study showed promising results—it reduced the number of *E. faecalis* bacteria in bacterial colonies.

4. Nanomaterials in Endodontic Instruments and Their Effects

Nickel-titanium (NiTi) endodontic rotary files are common instruments in dentistry today. Most of those available on the market are clockwise rotating instruments; only a few are counterclockwise-rotated with reciprocation movement, e.g., Reciproc® (VDW, München, Germany), Wave One® (Dentsply Sirona, Charlotte, USA). Practically all of them have a non-cutting tip, except Mtwo Retritment® (VDW, München, Germany), allowing one to file following the axis of the root canal or along the glide path. NiTi rotary files have different cross-sectional shapes which give them special properties. The smaller the cross-sectional area, the more flexible the tool and when the more acute angle at the edge, the cutting is better. Nitinol occurs in two crystalline phases (**Figure 4**) called martensite and austenite, and sometimes appears intermediate phase—R phase (e.g., Twisted Files). Their transformations (**Figure 5**) give particular properties, such as shape memory and superelasticity.

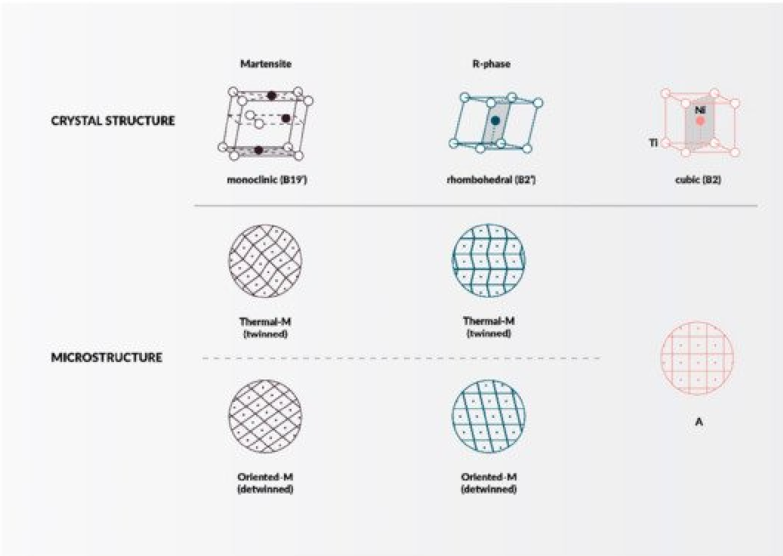


Figure 4. Different crystal structure phases and their microstructural characteristics.

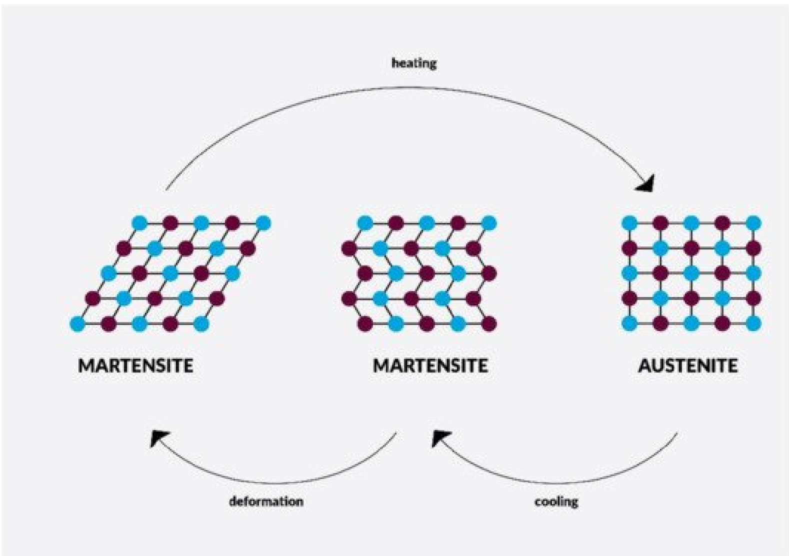


Figure 5. Graphic presentation of crystalline phases and their transformations.

The characteristic of martensite (low-temperature phase) is a crystal structure with lower symmetry, such as tetragonal, rhombohedral, orthorhombic, monoclinic, or triclinic structure. Martensitic transformations are potentially reversible and take place without diffusion or plasticity. It happens form solid to solid phase (in crystalline structure) under the influence of stress or when temperature is change. Files in this phase are very flexible, not very springy, and resistant to cyclic material fatigue but less resistant to deformations resulting from screwing in. The temperature at which martensite changes into austenite is similar to human body temperature, therefore in the case of extremely curved root canals, it is advisable to cool the tool to make it more flexible. The characteristics of another phase, austenite (high-temperature phase) is very symmetrical crystal structure. Files in this phase are more elastic, stiff, resistant to deformation as a result of screwing in but less resistant to cyclic material fatigue [78].

The new Self-adjusting File (SAF) technology (**Figure 6**) is kind of compressible, resilient NiTi net, and without central core. The SAF technology allows for the flow of irrigant, effective disinfection and adapts for any shape of root canals, e.g., oval canals. It removes as minimal layer of dentin from around of canal as it is needed and help avoid removal of healthy dentin and due to this it does not cause micro-cracks in root dentin [79].

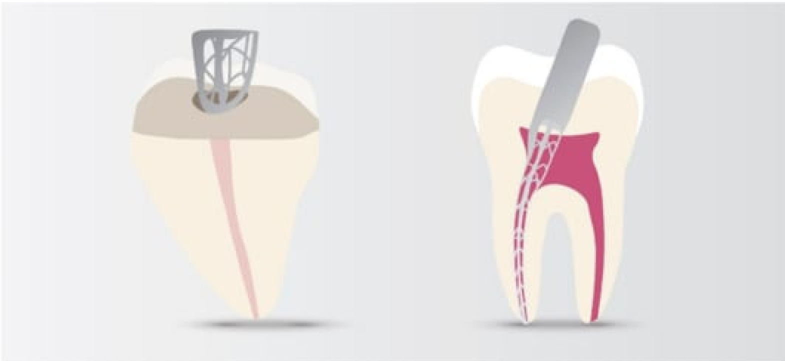


Figure 6. Self-adjusting File SAF technology visualization.

Another noteworthy NiTi rotary system is XP-Endo Finisher (**Figure 7**) whose revolutionary design enhances its ability to clean hard to reach places. It is characterized by extreme expansion capacity optimization up to 100× its core size, good adaptation for all root canals shapes, resistance to cyclic fatigue, flexibility and perfect removal of debris without removal significant amounts of good tissues.

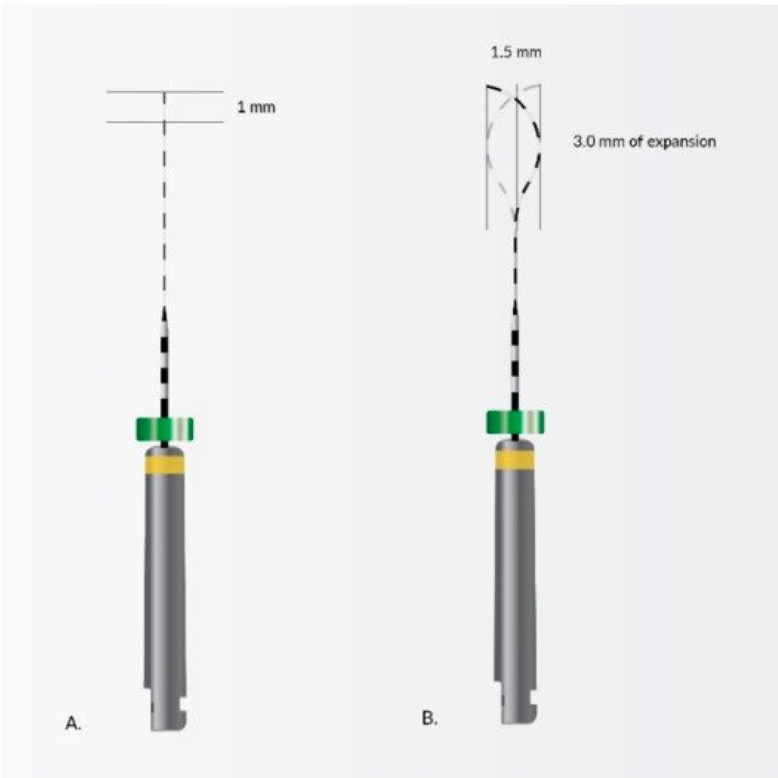


Figure 7. NiTi rotary system XP-Endo Finisher.

These types of alloys have beneficial properties such as high corrosion resistance and superelasticity due to this good shape memory [79][80][81]. Cobalt coatings of the NiTi file with impregnated fullerene-like WS2 nanoparticles significantly improve the fatigue resistance and breakage time.

5. Nanoapplications for Repair and Pulp Regeneration

A recent study by Fioretti et al. [82] tested the toxicity of nanostructured assemblies on dental pulp tissues, and the anti-inflammatory properties of alpha-melanocyte-stimulating hormone (MSH) were demonstrated. Their group have shown that the combination of substances with Poly-Glutamic Acid (PGA) with the incorporation of an anti-inflammatory hormone (melanocortin, a-MSH) into the multilayered Poly-L-Lysine (PLL)/PGA films increases the anti-inflammatory reaction of pulp fibroblasts (causing the proliferation of fibroblast cells) and macrophages stimulated by LPS (Lipo-Polysaccharides) [83]. These nanostructured assemblies are a reservoir of the anti-inflammatory peptide and promote the adhesion and proliferation of pulp fibroblasts on the biomaterial.

Smith IO et al. [84] and other researchers developed and examined nanostructured polymer scaffolds. They proved that the structural features of tissue engineering scaffolds affect cell response and must support cell adhesion, proliferation and differentiation. The test focused on nanofibrous (NF) scaffolds with combinations of components, which was similar to a synthetic extracellular matrix (ECM) interacting with cells before forming new tissue. Their group has developed biodegradable polymer arising in TIPS process to form NF with nanofibers with the same size and diameter as the collagen fibers found in the ECM (diameter 50–500 nm). This group has also grown apatite crystals onto biodegradable polymer scaffolds (by SBF), in which they changed the quantity and schedule of these crystals. Researchers are working on the schedule of these crystals throughout three-dimensional scaffolds (in both nano-fibrous and composite), to improve the ability of the cell to adhere, proliferate, and differentiate. It is also possible through growth and differentiation factors.

The production of an engineered replica of the naturally occurring ECM can promote the development of new tissue which is important for tissue repair and regeneration. Yang et al. [85] studied in vitro and in vivo behavior of dental pulp stem cells (DPSCs) on different scaffolds such as poly(epsilon-caprolactone) (PCL)/gelatin scaffolds with or without the addition of nano-hydroxyapatite (nHA). In the in vitro evaluation, DNA content, alkaline phosphatase (ALP) activity and osteocalcin (OC) measurement showed that the scaffolds supported DPSC adhesion, proliferation, and odontoblastic differentiation. In conclusion, the incorporation of nHA in nanofibers indeed enhanced DPSCs differentiation towards an odontoblast-like phenotype in in vitro and in vivo study models.

One study assessed the differentiation of human odontogenic DPSCs on NF poly L-lactic acid (PLLA) scaffolds. Wang J. et al. [86] show that odontogenic differentiation of DPSCs can be achieved on NF-PLLA scaffolds and the combination of BMP-7 and DXM induced the odontogenic differentiation more effectively than DXM alone. The NF-PLLA scaffold and the combined odontogenic inductive factors provide an excellent environment for DPSCs to regenerate dental pulp and dentin.

Gupte MJ et al. [87] with his group used highly permeable scaffolds of NF-PLLA (mimicked collagen type-I fibers) with and without the usage of the growth factors Bone Morphogenic Protein-7 (BMP-7) and dexamethasone (DXM) medium. It presented that mixing of the growth factor BMP-7 and DXM stimulated the differentiation of odontogenic DPSCs more effectively than DXM alone. The obtained environment was excellent support for DPSCs in regenerating dental pulp, dentin, and enamel.

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