FONDAZIONE ISTITUTO ITALIANO DI TECNOLOGIA

A TECHNOLOGY TEASER

COMBINED MATERIAL FOR DENTAL RECONDITION

ISTITUTO ITALIANO DI TECNOLOGIA

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NEW MATERIALS

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- promotes and develops scientific and technological excellence, both directly, through its multi-disciplinary research laboratories, and indirectly, through a wide collaboration with national and international laboratories and research teams;
- carries out advanced training programs as a part of wider multi-disciplinary projects and programs;
- fosters a culture based on sharing and valuing results, to be used in order to improve production and for welfare-related purposes, both internally and in relation to the entire national research system;
- creates technological understanding about components, methods, processes and techniques to be used for the implementation and interconnection of innovative products and services, in strategic areas for the competitiveness of the national production system;
- pools research scientists operating in various research institutes and establishes cooperation agreements with high-level, specialized centers;
- promotes interactions between basic research and applied research facilities, encouraging experimental development;
- spreads transparent, merit-based selection mechanisms for research scientists and projects, in compliance with globally approved and established criteria.

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EXECUTIVE SUMMARY

This document presents an overview of a set of technologies developed at IIT in the sector of the materials for dental restoration.
In the field of conservative dentistry, ample use is made of restorative dental materials, typically in cases in which cavities need to be filled due to caries removal or fractures. Said restorative dental materials must be able to bond stably to the dental surface, reproduce the behaviors of the original tissues as closely as possible, and be stable and resistant over time.

Scientists at IIT have developed a composite material which presents advantages and performances superior to the existing solutions.

This technology represents a unique chance for companies active in the market of dental products. IIT assets appear well positioned for an out-licensing strategy, providing the licensee partner with the ability to take care of the late stage development, CE certification, scale-up and production process. The licensee should guarantee a high probability of market success based on consolidated marketing & distribution organization. A typical licensing strategy based on entry fee and subsequent royalties on net sales can be envisaged.

INTELLECTUAL PROPERTY

PCT International Application #	PCT/IB2013/058809 - 24 September 2013
Priority Application #	MI2012A001634 - 01 October 2012
International Publication Date	10 April 2014
PCT National Phases	Nationalized in **EU** and **US** on April, 1st 2015
Applicant	Fondazione Istituto Italiano di Tecnologia
Inventors	Marco SALERNO, Sanjay THORAT, Alberto DIASPRO
Title	Combined material including anodic porous alumina and a polymer matrix, and its use for the dental recondition.

Short Description

The present invention relates to anodic porous alumina (APA) in the form of microparticles, characterized in that it contains interconnected through nanopores, and its use in the preparation of a new composite material, which is useful for example in the field of conservative dentistry. The invention further relates to a process for preparing the nanoporous alumina of the invention in microparticles.

The written opinion of the International Searching Authorities (received in January 2014) recognizes Novelty, Inventive step and Industrial applicability for all the claims (15).

IIT TECHNOLOGY

In the field of conservative dentistry, ample use is made of restorative dental materials, typically in cases in which cavities need to be filled due to caries removal or fractures. Said restorative dental materials must be able to bond stably to the dental surface, reproduce the behaviours of the original tissues as closely as possible, and be stable and resistant over time. The category of composite materials most used is that of so-called “hybrid” composite materials, which include a combination of inorganic fillers (consisting essentially of glass), covered by a silane coupling agent which joins them to a polymer matrix, and having a broad size distribution, from 10 nm to 10 µm. However, current restorative composite materials show a stability over time which is considerably inferior compared to amalgams, due in part to the chemical degradation of the filling material, and in part to hydrolysis of the silane coupling agent. Moreover, the degradation of the coupling agent, associated with the infiltrations that occur in the organic matrix, which is permeable to liquids coming from the surrounding environment (oral cavity), causes the release of polymer matrix and coupling material residues in the mouth, which in the long term can be a risk factor for the patient’s health.

Scientists at IIT have developed a composite material that is useful in dental restoration and comprises nanoporous alumina having interconnected through pores, in the form of microparticles, and a polymer matrix. Surprisingly, thanks to the mechanical interlace that is established between the microparticles of nanoporous alumina and the polymer matrix, the composite material of the invention does not require the use of any coupling agent, further ensuring excellent properties in terms of resistance, elasticity, biocompatibility and stability over time. In fact, the particular microparticulate form of the nanoporous alumina and the presence of interconnected through holes in each microparticle makes it possible to achieve an almost complete penetration of the polymer matrix into the alumina nanopores. In this manner the two components of the composite material are physically interconnected without there being a need to use any type of chemical coupling agent.

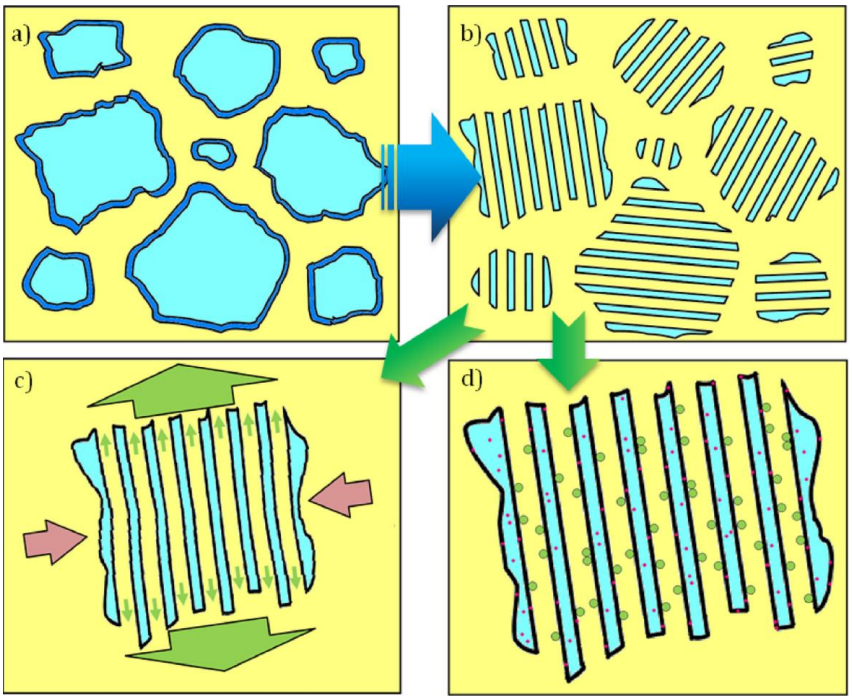


Figure 1. Sections of a filling composite: (a) traditional one, based on bulk fillers coated with bonding agent, and (b) IIT experimental one, based on porous fillers; (c and d) single porous filler close-up, showing possible strengthening and bioactive action, respectively.

According to the inventors, this technology is related to an anodic porous alumina (APA) having interconnected through nanopores having a diameter comprised between 20 and 300 nm, in the form of microparticles with a particle size of at least 5 microns, preferably comprised between 5 and 20 microns. APA is a nanostructured, inert, biocompatible, highly resistant and nontoxic material which can be easily prepared via controlled anodization of an electrode made of super-pure aluminium.

The anodic porous alumina according to the invention is therefore functionalized with at least one biologically active agent with antibacterial, disinfectant, mineralizing and/or regenerating properties. Specifically, the biologically active agent can be made by nanoparticles of silver, phosphate, fluoride, calcium or magnesium ions, proteins of the families of polylysine and extracellular matrix, integrin and laminin, vitronectin and fibronectin, bone morphogenetic protein (BMP) and growth factors.

The process for the formation of APA in the form of microparticles comprises three steps:

a) preparing a layer of APA by anodic oxidation of an aluminium, preferably superpure, electrode, immersed in an electrolytic solution;
b) forming a membrane of APA having interconnected through nanopores, by removing the residual aluminium substrate and subsequently by removing the bottom of the pores of the porous anodic alumina layer, and
c) grinding the alumina membrane of step b), obtaining APA microparticles having interconnected through nanopores.

The anodic porous alumina is therefore used in the preparation of a composite material by mixing APA with a well-known polymeric matrix generated from the monomers bisphenol-A diglycidyl methacrylate (Bis-GMA) and tetraethylenglycol dimethacrylate (TEGDMA), alone or in a mixture. Such a composite material is used as a filling material in dental recondition by applying the composite material in the tooth to be restored, and subsequently polymerizing said applied composite material.

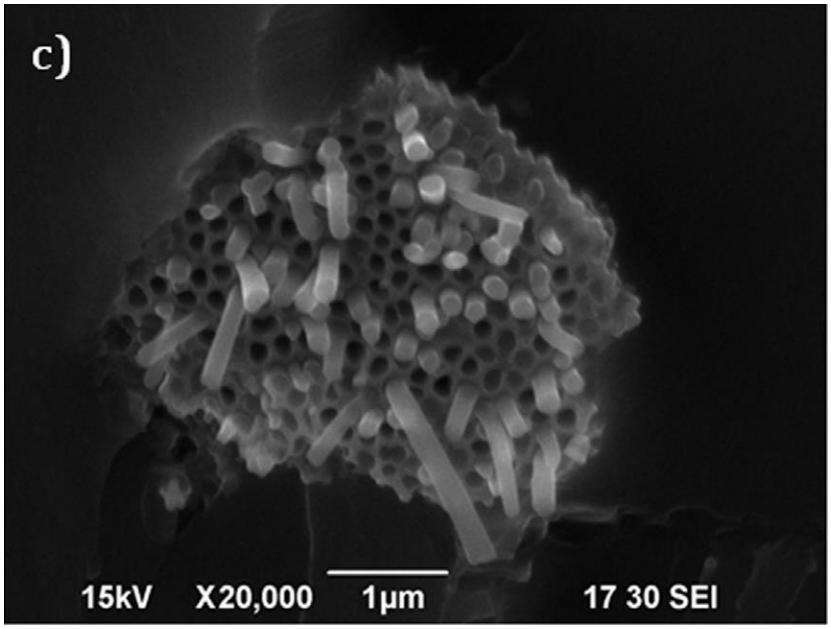


Figure 2. Typical SEM of a fractured surface of the IIT composite, which demonstrates the penetration of resin into the APA pores

MARKET ANALYSIS

Based on the IIT invention described in the PCT application PCT/IB2013/058809, internal documentation on the technology and related literature publications by the inventors and competitors, the **Dental Material Market**, which is a niche segment of the **Dental Supplies Market**, has been identified as the major reference marketplace. Accordingly, the Dental Material Market has been analyzed for its current dimension and future trends through a web search-based retrieval of specific information. Key players have been identified and their websites have been reported.

The Dental Material Marketplace

Dentistry is considered to be a branch of medicine, such as orthopedics or physiology or neurology. In fact, while based on common foundations of medicine, dentistry is a large stand-alone area, which has its own grasps to the different fields mentioned above. Indeed, the oral environment, which is the place where dental functions are operated, is one of the most complex ones in the human body. As a result, within the dental area several specialized disciplines exist (see Figure 3). *Conservative dentistry* aims to maintain the original denture and largely overlaps with *restorative dentistry*, the latter encompassing *prosthodontics*, *periodontics*, and *endodontics*. Prosthodontics (or prosthetic dentistry) is required in case of massive irreversible tooth damage that cannot be fixed with simple resin composite filling, and requires the use of prosthesis for teeth, namely crowns, bridges, and even whole dentures. Periodontics (or periodontology) addresses the diseases of the periodontum, i.e., the teeth ligaments. Endodontics focuses on therapy of the root canals and connected pulp diseases.

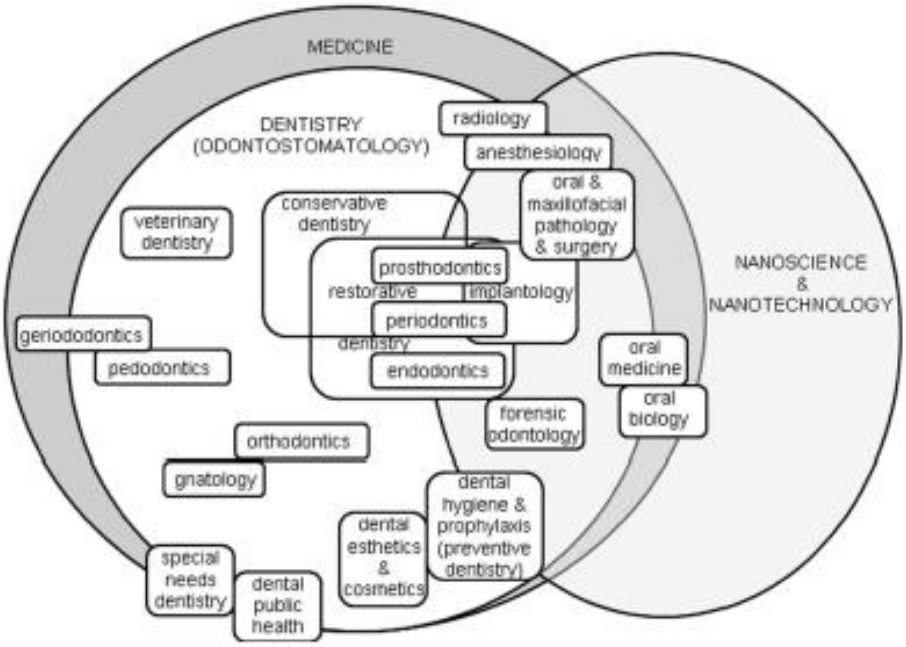


Figure 3. The dental arena, roughly contained in the area of medicine, and its specialties most likely connected to the advances in nanoscience and nanotechnology

Such a broad range of topics clearly makes use of a large spectrum of materials. In parallel, advanced technological solutions are required for the application of the underlying scientific principles. Actually, in dentistry, many special processes and practice protocols have been developed over the past century.

Dentistry is the area of medical sciences that is most resistant to the introduction of the novel methods arisen from the development of nanoscience and nanotechnology in the last 20 years. As a result, dentistry is separated from the other medical areas, and the recent integration of nanotechnology and nanoscience into dentistry is progressing more slowly than for general medicine.

Dental materials are specially fabricated materials, designed for use in dentistry. There are many different types of dental material, and their characteristics vary according to their intended purpose. Examples include temporary dressings, dental restorations (fillings, crowns, bridges), endodontic materials (used in root canal therapy), impression materials, prosthetic materials (dentures), dental implants, and many others.

Temporary dressings

A temporary dressing is a dental filling which is not intended to last in the long term. They are interim materials which may have therapeutic properties. A common use of temporary dressing occurs if root canal therapy is carried out over more than one appointment. In between each visit, the pulp canal system must be protected from contamination from the oral cavity, and a temporary filling is placed in the access cavity. Examples include:

- Zinc oxide eugenol - bactericidal, cheap and easy to remove. Eugenol is derived from oil of Cloves, and has an obtundant effect on the tooth and decreases toothache. It is a suitable temporary material providing there are no biting forces on it. It is also contraindicated if the final restorative material is composite because eugenol adversely effects the bond/polymerization process. Examples brands: Kalzinol™, Sedanol™.

Cements

Dental cements are used most often to bond indirect restorations such as crowns to the natural tooth surface. Examples include:

- Zinc oxide cement - self setting and harden when in contact with saliva. Example brands: Cavit™, Coltosol™.
- Polycarboxylate cement - Adheres to enamel and dentin. Example brands: PolyF™.

Impression materials

Dental impressions are negative imprints of teeth and oral soft tissues from which a positive representation can be cast. They are used in prosthodontics (to make dentures), orthodontics, restorative dentistry, dental implantology and oral and maxillofacial surgery. Impression materials are designed to be liquid or semi-solid when first mixed, then set hard in a few minutes, leaving imprints of oral structures. Common dental impression materials include sodium alginate, polyether, and silicones. Historically, plaster of Paris, zinc oxide eugenol, and agar have been used.

Restorative materials

Glass ionomer cement (GIC) - composite resin spectrum of restorative materials used in dentistry. Towards the GIC end of the spectrum, there is increasing fluoride release and increasing acid-base content; towards the composite resin end of the spectrum, there is increasing light cure percentage and increased flexural strength.

Dental restorative materials are used to replace tooth structure loss, usually due to dental caries, but also tooth wear and dental trauma. On other occasions, such materials may be used for cosmetic purposes to alter the appearance of an individual's teeth.

There are many challenges for the physical properties of the ideal dental restorative material. The goal of research and development in restorative materials is to develop the ideal restorative material. The ideal restorative material would be identical to natural tooth structure in strength, adherence, and appearance. The properties of an ideal filling material can be divided into four categories: physical properties, biocompatibility, aesthetics and application.

- Requisite physical properties include low thermal conductivity and expansion, resistance to different categories of forces and wear such as attrition and abrasion, and resistance to chemical erosion. There must also be good bonding strength to the tooth. Everyday masticatory forces and conditions must be withstood without material fatigue.
- Biocompatibility refers to how well the material coexists with the biological equilibrium of the tooth and body systems. Since fillings are in close contact with mucosa, tooth, and pulp, biocompatibility is very important. Common problems with some of the current dental materials include chemical leakage from the material, pulpal irritation and less commonly allergy. Some of the byproducts of the chemical reactions during different stages of material hardening need to be considered.
- Ideally, filling materials should match the surrounding tooth structure in shade, translucency, and texture.
- Dental operators require materials that are easy to manipulate and shape, where the chemistry of any reactions that need to occur are predictable or controllable.

Direct restorative materials

Direct restorations are ones which are placed directly into a cavity on a tooth, and shaped to fit. The chemistry of the setting reaction for direct restorative materials is designed to be more biologically compatible. Heat and byproducts generated cannot damage the tooth or patient, since the reaction needs to take place while in contact with the tooth during restoration. This ultimately limits the strength of the materials, since harder materials need more energy to manipulate. The type of filling (restorative) material used has a minor effect on how long they last. The majority of clinical studies indicate the annual failure rates (AFR's) are between 1% and 3% with tooth colored fillings on back teeth. Note that root canaled (endodontically) treated teeth have AFR's between 2% and 12%. The main reasons for failure are cavities that occur around the filling and fracture of the real tooth. These are related to personal cavity risk and factors like grinding teeth (bruxism).

Amalgam - Amalgam is a metallic filling material composed from a mixture of mercury (from 43% to 54%) and powdered alloy made mostly of silver, tin, zinc and copper, commonly called the amalgam alloy. Amalgam does not adhere to tooth structure without the aid of cements or use of techniques which lock in the filling, using the same principles as a dovetail joint. Amalgam is still used extensively in many parts of the world because of its cost effectiveness, superior strength and longevity. However, the metallic colour is not aesthetically pleasing and tooth coloured alternatives are continually emerging with increasingly comparable properties. Due to the known toxicity of the element mercury, there is some controversy about the use of amalgams. The Swedish government banned the use of mercury amalgam in June 2009. Research has shown that, while amalgam use is controversial and may increase mercury levels in the human body, these levels are below safety threshold levels established by the WHO and the EPA. However, there are certain subpopulations who, due to inherited genetic variabilities, exhibit sensitivity to mercury levels lower than these threshold levels. These particular individuals may experience adverse effects caused by amalgam restoration. These include myriad neural defects, mainly caused by impaired neurotransmitter processing.

Composite resin - Composite resin fillings (also called white fillings) are a mixture of powdered glass and plastic resin, and can be made to resemble the appearance of the natural tooth. Although cosmetically superior to amalgam fillings, composite resin fillings are usually more expensive. Bis-GMA based resins contain Bisphenol A, a known endocrine disrupter chemical, and may contribute to the development of breast cancer. However, it has been demonstrated that the extremely low levels of bis-GMA released by composite restorations do not cause a significant increase in markers of renal injury, when compared to amalgam restorations. That is, there is no added risk of renal or endocrine injury in choosing composite restorations over amalgams. Most modern composite resins are light-cured photopolymers, meaning that they harden with light exposure. They can then be polished to achieve maximum aesthetic results. Composite resins experience a very small amount of shrinkage upon curing, causing the material to pull away from the walls of the cavity preparation. This makes the tooth slightly more vulnerable to micro-leakage and recurrent decay. Micro-leakage can be minimized or eliminated by utilizing proper handling techniques and appropriate material selection.

In some circumstances, less tooth structure can be removed compared to preparation for other dental materials such as amalgam and many of the indirect methods of restoration. This is because composite resins bind to enamel (and dentin too, although not as well) via a micromechanical bond. As conservation of tooth structure is a key ingredient in tooth preservation, many dentists prefer placing materials like composite instead of amalgam fillings whenever possible.

Generally, composite fillings are used to fill a carious lesion involving highly visible areas (such as the central incisors or any other teeth that can be seen when smiling) or when conservation of tooth structure is a top priority. The bond of composite resin to tooth, is especially affected by moisture contamination and cleanliness of the prepared surface. Other materials can be selected when restoring teeth where moisture control techniques are not effective.

Glass Ionomer Cement - The concept of using “smart” materials in dentistry has attracted a lot of attention in recent years. Conventional glass-ionomer (GI) cements have a large number of applications in dentistry. They are biocompatible with the dental pulp to some extent. Clinically, this material was initially used as a biomaterial to replace the lost osseous tissues in the human body. These fillings are a mixture of glass and an organic acid. Although they are tooth-colored, glass ionomers vary in translucency. Although glass ionomers can be used to achieve an aesthetic result, their aesthetic potential does not measure up to that provided by composite resins. The cavity preparation of a glass ionomer filling is the same as a composite resin. However, one of the advantages of GI compare to other restorative materials is that they can be placed in cavities without any need for bonding agents. Conventional glass ionomers are chemically set via

an acid-base reaction. Upon mixing of the material components, there is no light cure needed to harden the material once placed in the cavity preparation. After the initial set, glass ionomers still need time to fully set and harden.

Advantages:

1. Glass ionomer can be placed in cavities without any need for bonding agents.

2. They are not subject to shrinkage and micro-leakage, as the bonding mechanism is an acid-base reaction and not a polymerization reaction. GICs do not undergo great dimensional changes in a moist environment in response to heat or cold and it appears heating results only in water movement within the structure of the material. These exhibit shrinkage in a dry environment at temperature higher than 50°C, which is similar to the behavior of dentin.

3. Glass ionomers contain and release fluoride, which is important to preventing carious lesions. Furthermore, as glass ionomers release their fluoride, they can be "recharged" by the use of fluoride-containing toothpaste. Hence, they can be used as a treatment modality for patients who are at high risk for caries. Newer formulations of glass ionomers that contain light-cured resins can achieve a greater aesthetic result, but do not release fluoride as well as conventional glass ionomers.

Disadvantages:

The most important disadvantage is lack of adequate strength and toughness. In an attempt to improve the mechanical properties of the conventional GI, resin-modified ionomers have been marketed. GICs are usually weak after setting and are not stable in water; however, they become stronger with the progression of reactions and become more resistant to moisture. New generations: the aim is tissue regeneration, and use of biomaterial in the form of a powder or solution is to induce local tissue repair. These bioactive materials release chemical agents in the form of dissolved ions or growth factors such as bone morphogenetic protein (BMP), which stimulates activate cells.

Glass ionomers are about as expensive as composite resin. The fillings do not wear as well as composite resin fillings. Still, they are generally considered good materials to use for root caries and for sealants.

Resin modified Glass-Ionomer Cement (RMGIC) - A combination of glass-ionomer and composite resin, these fillings are a mixture of glass, an organic acid, and resin polymer that harden when light cured (the light activates a catalyst in the cement that causes it to cure in seconds). The cost is similar to composite resin. It holds up better than glass ionomer, but not as well as composite resin, and is not recommended for biting surfaces of adult teeth.

Generally, resin modified glass-ionomer cements can achieve a better aesthetic result than conventional glass ionomers, but not as good as pure composites. It has its own setting reaction.

Compomers - Another combination of composite resin and glass ionomer technology, with focus lying towards the composite resin end of the spectrum. Although compomers have better mechanical and aesthetic properties than RMGIC, they have worse wear properties and require bonding materials. Although compomers release fluoride, they do so at such a low level that it is not deemed effective, and unlike glass ionomer and RMIC, cannot act as a fluoride reservoir.

Dental Restorative Nanomaterials - One major field of application of nanotechnology to dentistry is the fabrication of dental restorative composites. In recent years, several composites claimed to be "nano," such as Filtek Supreme™ (FS) by 3M-ESPE and Venus Diamond™ (VD) by Heraeus Kulzer. The latter in particular is an advanced formulation of hybrid composite, using filler particles with multiple size populations across both the micro- and the nanoscale.

Indirect Restorative materials

Indirect restorations are ones where the tooth or teeth to receive the restoration are first prepared, then a dental impression is taken and sent to a dental technician who fabricates the restoration according to the dentist's prescription.
Porcelain (ceramic) - Porcelain fillings are hard, but can cause wear on opposing teeth. They are brittle and are not always recommended for molar fillings.

Composite Resin - Tooth colored dental composite materials are either used as direct filling or as construction material of an indirect inlay. It is usually cured by light.

Ceramic-Resin Hybrids - Nano-ceramic particles embedded in a resin matrix, they are less brittle and therefore less likely to crack, or chip, than all-ceramic indirect fillings; they absorb the shock of chewing more like natural teeth, and more like resin or gold fillings, than do ceramic fillings; and at the same time more resistant to wear than all-resin indirect fillings. These are available in blocks for use with CAD-CAM systems.

Gold - Gold fillings have excellent durability, wear well, and do not cause excessive wear to the opposing teeth, but they do conduct heat and cold, which can be irritating. There are two categories of gold fillings, cast gold fillings (gold inlays and onlays) made with 14 or 18 kt gold, and gold foil made with pure 24 kt gold that is burnished layer by layer. For years, they have been considered the benchmark of restorative dental materials. Recent advances in dental porcelains and consumer focus on aesthetic results have caused demand for gold fillings to drop in favor of advanced composites and porcelain veneers and crowns. Gold fillings are sometimes quite expensive; yet, they do last a very long time - which can mean gold restorations are less costly and painful in the long run. It is not uncommon for a gold crown to last 30 years.

Failure of dental restorations

Fillings have a finite lifespan: an average of 12.8 years for amalgam and 7.8 years for composite resins. However, the lifespan of a restoration also depends upon how the patient takes care of the offended tooth which was restored and do not exert too much pressure by eating hard food substances.

Evaluation and regulation of dental materials

The Nordic Institute of Dental Materials (NIOM) evaluates dental materials in the Nordic countries. This research and testing institution are accredited to perform several test procedures for dental products. In Europe, dental materials are classified as medical devices according to the Medical Devices Directive. In USA, the Food and Drug Administration is the regulatory body for dental products.

Dental Supplies Market

As already mentioned above, the Dental Materials Market is a niche segment of the greater Dental Supplies Market. According to the research report titled *"Dental Supplies: A Global Strategic Business Report"* published in 2011 by Global Industry Analysts Inc., the **global market for Dental Supplies is projected to reach US$ 19.4 billion by the year 2017** (http://www.biomedtrends.com/GetDetails.asp?CatName=Dental), driven by an aging population, increasing awareness about oral care, rise in demand for preventive and cosmetic dental procedures and technological developments. Rising per capita spending across developed countries and increasing discretionary incomes in developing countries are driving global growth.

Dental supplies account for the largest share of the overall dental market comprising consumables and implants, equipment and services. The segment includes products used in dental procedures such as amalgams and alloys, prosthetic and aesthetic supplies, orthodontic supplies, endodontic supplies, dental implants and infection control products. The economic crisis took its toll on the dental supplies industry as the market experienced a sharp decline in sales in recent years. This was attributed primarily to a decline in patient traffic, as patients deferred or postponed treatment that further led to a fall in purchases of supplies by dentists and dental laboratories. The increasing rate of unemployment, contracting household incomes, and reduced access to credit all led to slowdown in patient traffic to dental clinics. In particular, several patients avoided dental implant procedures, which involve the use of biomaterials such as tissue regeneration products, dental membrane and bone graft substitutes, and chose relatively inexpensive alternatives such as bridges or crowns. As a result, sales of biomaterials fell considerably.

Despite the rebounding in economy, dental supplies industry still awaits full recovery in volumes and is not expected to reach the pre-recession levels in the immediate future. Demand for dental products and services is expected to grow in the long run driven by the growing awareness about oral healthcare, favorable demographic profile, increase in the number of people opting for cosmetic treatment, and introduction of new products that reduce patient discomfort. The market continues to witness the introduction of procedures and solutions that are making the process of dental surgery less invasive and less time consuming. Efforts are focused on the prevention of dental ailments, which is in turn driving demand for restorative and repair materials. New products are aimed at reducing patient discomfort, shorten healing time and provide improved functioning. Patients and dentists are increasingly adopting dental membrane materials, tissue regeneration and dental bone graft materials as highly advanced versions of these products are being developed. Further, surgeons are growing more aware of the available biological products that are designed for orthopedic applications.

As stated by the research report on Dental Supplies, the US continues to remain the single largest regional market. Asia-Pacific is set to grow at the fast compounded annual growth rate of 8.9% over the analysis period. The low penetration of the dental market in potential markets such as India presents tremendous potential for future growth. Prosthetic Supplies represents the largest segment in the global dental supplies market. Comprising products such as crowns, bridges, and dentures among others, prosthetic supplies represent the conventional form of treatment for majority of the dental ailments. The focus on preventive dentistry as well as procedures such as periodontics, endodontics, and orthodontics, which allow patients to retain their natural teeth longer, is also expected to fuel demand for dental products. In the dental bridge and crown restoration segment, introduction of new technologies and materials to be used alongside dental bridges and crowns, and substantial efforts to promote benefits of computer-aided manufacturing/ computer-aided design (CAM/CAD) technology are expected to drive the market.

Dental Implants segment is forecast to grow at the fastest compounded annual rate of 10.6% over the analysis period. Growth in the dental implants market is driven by growing awareness and demand for improved oral aesthetics. In addition, factors such as technological improvements and the growing acceptance of the procedure as a cost effective option relative to alternative treatments is expected to fuel sales of dental implants. Edentulous patients increasingly prefer dental implants as they are easy to use. In

addition, advancements in dental implants technology which reduce treatment times considerably are expected to contribute to the growth.

Dental Materials Market

US Dental Materials Market

According to a recent report published by Research and Markets in December 2013, titled *"US Market for Dental Materials",* the US market for dental materials is a dynamic industry with **a market value of over US$ 1 billion as of 2013; this market is expected to grow substantially and to approach US$ 1.5 billion by 2020** (http://www.researchandmarkets.com/reports/2765778/u_s_market_for_dental_materials#relb0). The dental materials market is composed of segments for dental cements, impression materials, direct restorative materials (composites, for example), bonding agents, core build-up materials and dental local anesthetics. More than a dozen dental material companies operated in at least four of these segments in 2013, contributing to the already relentless competition in research and development, market and unit share, and product prices. Dental materials continuously show technological advancements that facilitate the workflow of dentists and increase the comfort of patients. As such, smaller niche companies can capture significant market share over a short period of time when they introduce a new product. These factors contribute to the fast- changing nature of the dental materials market, making it a very dynamic, exciting industry to follow and forecast. While the market for impression materials is expected to contract owing to the introduction of intra-oral digital impression scanners, positive growth in other segments will more than make up for the value loss. In 2013, the dental cement market experienced the fastest growth rate. Materials such as zinc polycarboxylate and zinc phosphate have given way to more esthetic and easy-to-use materials, such as composite resin and glass ionomer and resin-modified glass ionomer cement. This trend will continue through 2020, by the end of which composites will make up more than half of all dental cement unit sales.

The demise of traditional impression materials and the rise of intra-oral digital impression scanners

In 2013 there were eight intra-oral digital impression scanners on the US market, with four new devices on their way to commercialization. Even though the intra-oral digital impression scanner market for dentists is still in its infancy, the growth potential is undeniable. This market is expected to grow at a compound annual growth rate of over 10% through 2020. It is estimated that approximately 15% of dental offices owned a chairside milling system that came with a scanner in 2013. In addition to those, stand-alone scanners, which are much cheaper compared with chairside systems, are gaining traction, even in smaller dental offices. The advantages of these scanners include greater comfort for the patient, higher precision and a significant reduction in the number of retakes. These developments are projected to have substantial impact on the dental impression materials market. Even though new and better impression-taking products are being developed by large competitors, such as 3M ESPE, Dentsply International, Heraeus Kulzer, Parkell and Kettenbach, the advent of digital impression taking will slowly replace traditional impression materials. It should be noted that impression materials will never completely be removed from dental offices, as dentists will keep them on hand as an alternative to the digital method in case of electronic failures. However, this will not be sufficient to justify the presence of a multitude of companies in the market. We anticipate that this market will experience substantial consolidation over the next decade.

Increasing popularity of direct restoratives propelled by continuing growth in the composite segment

Direct dental restoratives have been going through a major transformation for some time, switching from amalgam to more esthetically pleasing restoratives, such as composites. Although the use of amalgam continues to be approved by both the American Dental Association and Food and Drug Administration for dental procedures, the backlash against this material based on environmental and health concerns has had an impact on its sales, despite a lack of scientific data to link it to health hazards. Yet, the fatal blow to the amalgam market was delivered by the increasing concern for dental esthetics; amalgam's silver coloring does not fare well with the contemporary understanding of dental elegance.

In contrast, composite materials provide a wide range of shades that can easily be matched to the natural color of teeth. They also show excellent bonding strength and preserve more natural tooth than amalgam. These factors have contributed to the increasing popularity of composites, notwithstanding higher prices and lack of durability compared with amalgam. These trends will dictate the future of the direct restorative materials market over the next decade, as a significant expansion is projected through 2020.

Bonding agents: Universal etch is gaining market share despite confusion over the meaning of "universal"

The latest development in the bonding agent market was the introduction of Universal etch systems in 2012. Universal etch systems are considered the eighth generation of bonding agents: they can be used either in the self-etch or total-etch capacity, depending on the application. Different universal bonding agents claim universality in a variety of ways, including applicability to all surfaces and exchangeability between total - vs. self-etch modes. It is difficult to find one truly universal agent. Moreover, some dentists still prefer to use total etch for certain applications, such as enamel bonding and self-etch for dentin.

Resistance to change, proven efficiency and bond strength of self- and total-etch agents, and the slightly higher price tag of universal bonding agents are factors limiting the adoption rate. Notwithstanding, these universal agents are the next big thing in the bonding agent market; as such, dentists are increasingly trying out and using universal bonding agents in restorative procedures. Lastly, with data showing that universal agents provide satisfactory bond strength, even in the presence of saliva, these agents appear to have it all. In 2013 universal bonding agents increased their market share significantly, and they will continue their journey toward becoming the most widely used bonding agent in dental offices during the next few years.

Dental materials will continue to characterize an exciting market for technological advancements, market growth and fierce competition

Dental materials have exhibited high levels of price and technological competition among manufacturers. However, much of the market has been largely dominated by 3M ESPE, Dentsply International and Kerr Corporation. Still, smaller companies have been successful in niche segments with alternative products and reasonable prices. Bisco, Tokuyama Dental, Kuraray and Kettenbach were especially noteworthy in marketing products that captured dentists' attention. The markets for restorative composites, core buildup materials and dental cements constituted a higher number of manufacturers, albeit with very small market shares for many. Other segments had fewer competitors and exhibited higher levels of concentration, such as anesthetics and glass ionomer and resin-modified glass ionomer cements. Private labeling was a large force in segments such as anesthetics and impression materials, reflecting the cost sensitivity of the customer base in 2013. Overall, the dental materials industry will remain a vibrant one for manufacturers in terms of profitability and abounding opportunities in the foreseeable future.

European Dental Materials Market

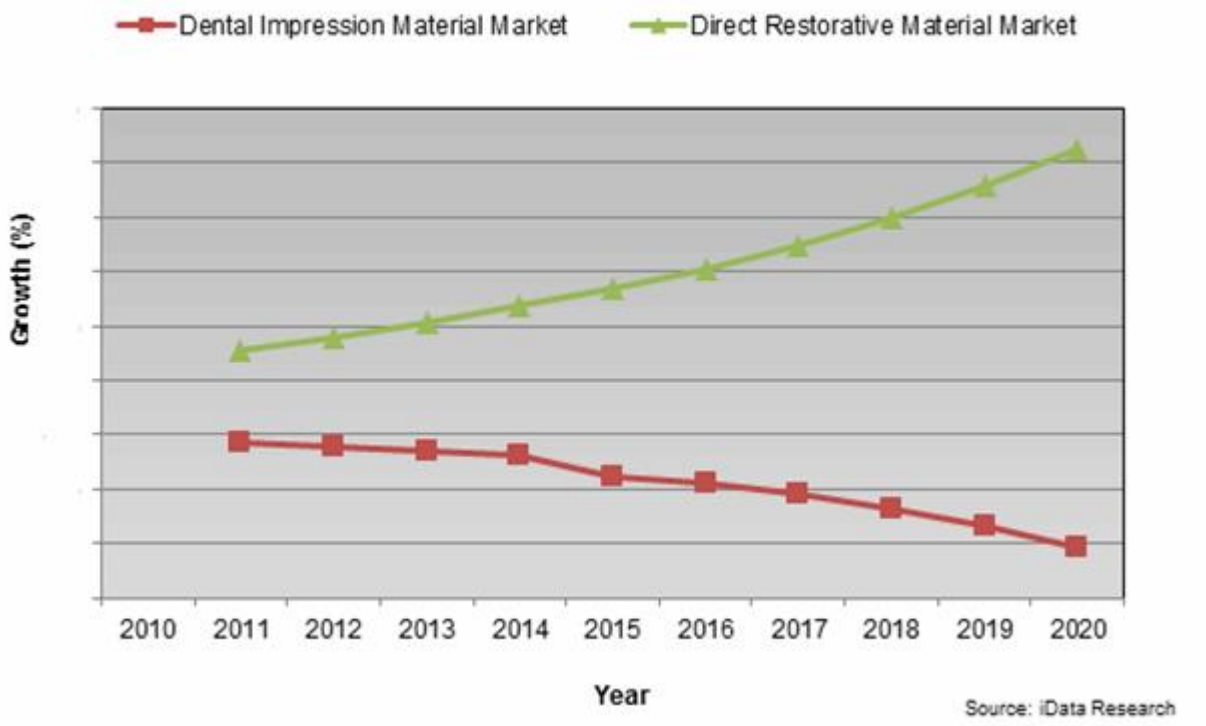
According to a new report by iData Research published in February 2015, **composite dental filling material, despite being more costly, has become the European dental filling of choice** (http://www.idataresearch.com/european-dental-materials-market/). The aesthetically pleasing nature of the material caters to growing trends towards cosmetic dentistry. The composite market, as a whole, has been gaining momentum, and will continue to do so as composite serves as the most viable alternative to amalgam dental fillings. *"Composites represented the largest portion of the European direct restorative market in 2014, valued at over €400 million*" explains Dr. Kamran Zamanian, CEO of iData. *"Growth in the overall direct restorative market has been driven by the rising popularity of composite resin materials as the preferred substance for fillings sold across dental clinics in Europe."* (http://globenewswire.com/news-

release/2015/02/03/702669/10118492/en/3M-ESPE-Rides-the-Success-of-Composite-Resin-Dental-Restorative-Sales-in-Europe.html).

Changing Consumer Preferences Generate 'Pull' Demand for Restorations – Notably, in supporting the restructuring of the market are consumer expectations and preferences. These preferences include increased emphasis on environmental concerns and safety hazards, greater importance on dental aesthetics, preference towards minimally invasive dentistry, and higher expectations placed on patient comfort.

The first three demands mentioned all point to the growth of resin-based materials. Amalgam, which was the original and long-lived inexpensive gold standard for restorative procedures (both direct and indirect), is now being phased down and even out in several regions across Europe. The initial catalyst for this shift has been the growing awareness and concern of mercury contained in amalgam, which has posed an environmental threat and potential safety hazard to patients. However, this alone does not suffice as the sole purpose for amalgam disappearing from the market. In line with this trend is the fact that consumers are placing more importance on the aesthetics of their teeth. This has been demonstrated through greater demand for whitening procedures and veneer placements.

Resin-based materials are now catering to this need and are growing to be offered in a variety of colors that guarantee the utmost aesthetic qualities. Composite resin and resin modified glass ionomer (RMGI) materials are further being promoted as customers are demanding less-invasive treatments that conserve more of their natural tooth. The growth pattern of the restorative market is consequently as follows: the amalgam market will be declining at a CAGR of over 13% across Europe over the course of the next 6 years, while composite resin products will be growing at a CAGR of over 8%. The shift in the market has been and will continue to be dramatic over the next decade, boosting the various restorative markets forward in terms of market value (this includes cements, core buildups, and filling materials). The overall restorative market will consequently grow and reach a value of over €800 million across Europe in 2020.



Demographic Factors - Older generations are likely to return to the dentist to have an older, fractured filling replaced. As Europe's aging population increases, the number of dental restorations necessary is set to grow. Europeans are also visiting the dentist to have their amalgam fillings replaced by composite resin. Consequently, demand for restoratives is set to rise. The trend towards less invasive treatments aligns with the trends towards composite resin and direct restorative treatments. Comparatively, the traditional amalgam fillings require a more invasive procedure; a greater portion of natural tooth is lost.

COMPETITIVE SCENARIO

Leading Players in the Dental Supplies Market

The market for dental supplies is highly fragmented although a handful of players enjoy long presence in several segments. Major players in the marketplace include:

- 3M ESPE (USA, http://solutions.3m.com/wps/portal/3M/en_WW/3MESPE/worldwide/),
- Align Technology Inc. (USA, http://www.aligntech.com/),
- BioHorizons (USA, http://www.biohorizons.com/contact.aspx),
- Biomet 3i Inc. (USA, http://www.biomet3i.com/),
- Camlog AG (Switzwrland, http://www.camlog.com/en/),
- Church & Dwight (USA, http://www.churchdwight.com/),
- Colgate-Palmolive (USA, http://www.colgate.it/app/Colgate/IT/HomePage.cvsp),
- Danaher Corporation (USA, http://www.danaher.com/),
- Den-Mat Corporation (USA, http://www.denmat.com/),
- Dental Services Group (USA, http://www.dentalservices.net/),
- Dentsply International Inc. (USA, https://www.dentsply.com/content/dentsply/en/website.html),
- DMG Hamburg GmbH (Germany, http://de.dmg-dental.com/start.de/),
- GC Corporation (USA, http://www.gc-dental.com/),
- GlaxoSmithKline CH (UK, http://www.gsk.com/en-gb/products/our-consumer-healthcare-products/),
- Heraeus Kulzer GmbH(Germany, http://heraeus-kulzer.com/en/int/home_4/worldmap_2014.aspx),
- Ivoclar Vivadent AG (Liechtenstein, http://www.ivoclarvivadent.com/),
- Laboratoire Septodont (France, http://www.septodont.fr/),
- Keystone Dental Inc. (USA, http://www.keystonedental.com/),
- MIS Implants Technologies Ltd. (Israel, http://www.mis-implants.com/MIS-Info.aspx),
- Nobel Biocare AB (Sweden, https://www.nobelbiocare.com/international/en/home.html),
- Osstem Implant (Korea, http://en.osstem.com/),
- Pfizer CH (USA, http://www.pfizer.com/partnering/areas_of_interest/consumer_healthcare),
- Proctor & Gamble (USA, http://www.pg.com/it_IT/),
- Shofu Inc. (Japan, http://www.shofu.com/),
- Straumann AG (Switzerland, http://www.straumann.com/),
- Sure Dent Corporation (Korea, http://sure-endo.en.ec21.com/company_info.jsp),
- Sweden & Martina SpA (Italy, http://www.sweden-martina.com/index.php?lang=1),
- SybronEndo corporation (USA, http://www.sybronendo.com/),
- VOCO GmbH (Germany, http://www.voco.de/landingpage/index.html),
- Zimmer Dental Inc. (USA, http://www.zimmerdental.com/Home/zimmerDental.aspx).

Leading Players in the Dental Materials Market (US and EU)

- 3M ESPE (USA, http://solutions.3m.com/wps/portal/3M/en_WW/3MESPE/worldwide/),
- Bisco Inc. (USA, https://www.bisco.com/),
- Carestream (USA, http://www.carestreamdental.com/us/en/company/About%20Us#AboutUs),
- Coltene/Whaledent Inc. (USA, http://www.coltene.com/index_en.php),
- Cosmedent Inc. (USA, http://www.cosmedent.com/),
- DMG Hamburg GmbH (Germany, http://de.dmg-dental.com/start.de/),
- Den-Mat Corporation (USA, http://www.denmat.com/),
- Dentsply International Inc. (USA, https://www.dentsply.com/content/dentsply/en/website.html),
- Dux Dental (USA, http://www.duxdental.com/),
- GC America (USA, http://www.gcamerica.com/),
- GC Europe (Belgium , http://www.gceurope.com/),
- Heraeus Kulzer GmbH (Germany, http://heraeus-kulzer.com/en/int/home_4/worldmap_2014.aspx)
- Ivoclar Vivadent AG (Liechtenstein, http://www.ivoclarvivadent.com/),
- Kettenbach (Germany, http://www.kettenbach.de/),
- Kerr Corporation USA, http://www.kerrdental.com/),
- KerrHawe (Switzerland, http://www.kerrhawe.com),
- KaVoKerr Group (USA, http://www.kavokerrgroup.com/),
- Kuraray (Japan, http://www.kuraray-dental.eu/it),
- Kuraray Noritake Dental Inc. (Japan, http://www.kuraraynoritake.com/),
- Parkell (USA, http://www.parkell.com/),
- Pentron Clinical Technologies (USA, http://www.pentron.com/),
- Pierrel SpA (Italy, http://www.pierrelgroup.com/modules/core/page.asp?p=HOME),
- Premier Products Company (USA, http://www.premusa.com/home/default.asp),
- Septodont (USA, http://www.septodont.com/),
- Shofu Inc. (Japan, http://www.shofu.com/),
- Silmet Ltd. (Israel, http://silmetdental.com/contact.aspx),
- Straumann AG (Switzerland, http://www.straumann.com/),
- Tokuyama Dental (Japan, http://www.tokuyama-dental.com/),
- Ultradent (USA, https://www.ultradent.com/en-us/Pages/default.aspx),
- VOCO GmbH (Germany, http://www.voco.de/landingpage/index.html).

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