From Production Skills to Scientific Knowledge,
and Onward to Fusion with Medical Science

TMR-Z Fill 10.
Product Report

Composite Resin: In Pursuit of Sustained Fluoride Release, High Strength and Operability

Edited by YAMAKIN Ph.D. Group

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What is the YAMAKIN Ph.D. Group?
This is a group of experts in various specialized fields who combine their knowledge, experience and technical expertise to act as a prime mover in the continuous generation of innovation.

TMR-Z Fill 10. Product Report

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1. Introduction

Restorative treatment for dental caries using composite resin is a method that achieves the treatment of healthy dentin with the least possible grinding or machining. Also, since composite resin is an effective filling material for easily adjusting the color tone to surrounding natural teeth, it is a material that satisfies the demand over recent years for the "restoration of white teeth."

Moreover, composite resin is an organic-inorganic complex material consisting of monomers which are made into macromolecules by curing, and inorganic fillers surface-treated with a silane coupling agent. It has become used for a wide range of cases in dental treatment thanks to a combination of its relatively low price among controlled medical devices and the spread of the concept of MI (Minimal Intervention) treatment in recent years. Composite resins with such characteristics include a universal type, which has excellent formability, and a flowable type with high flowability. In recent years, the flowable type which easily fills a wide range of cavities, is used more frequently.

Although this kind of composite resin has the above characteristics, there are issues regarding its strength compared to metal and ceramic materials. This is especially true since the concept of MI treatment has been refined. MI treatment is now used not only for treating small caries on the dentine surface layer, but also for repairing the crown of the molar. Thus, high strength which can withstand occlusion is required of composite resins.

Furthermore, in addition to having the requisite strength, composite resin needs to be comprehensively excellent from the viewpoints of durability, operability, color tone, and sustained fluoride release, among other qualities. Especially for operability, rheology (formability and fluidity) which does not place a burden on the operator is required, and for color tone, it is desirable that the color tone of natural teeth can be easily reproduced. Sustained fluoride release has been proposed for the prevention of secondary caries, and sustained release and rechargeability are considered effective.

TMR-Z Fill 10.

In responding to such demands, it is difficult to satisfy all the requirements. For example, a dental material with a sustained fluoride release property may suffer a decrease in strength and color tone depending on the sustained release process of fluoride ions. YAMAKIN CO., LTD. (referred to as YAMAKIN) has undertaken product development with the focus on "sustained fluoride release" and "strength" for the required tasks.
As a result, we are now offering a new composite resin in our line-up. "TMR-Z Fill 10." appropriately combines sustained fluoride release property and the YAMAKIN technology "Ceramics Cluster Filler," which is employed for both the hybrid composite resin "TWiNY" and the resin block series for CAD/CAM. In this way, under the concept of achieving both high strength that can be used for occlusal surfaces and sustained fluoride release, this product has been realized by putting various technologies for resin material together, with special consideration for the particularly required qualities of operability and color tone.

In this product report, "TMR-Z Fill 10." will be introduced from various angles. We hope that you will be interested in this product and avail of its outstanding features in future dental treatments.

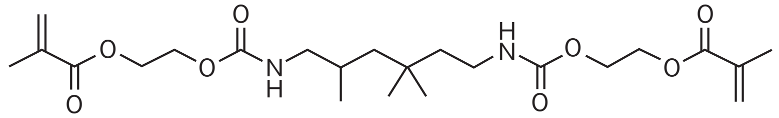
2. Basic Points about Composite Resin for Dental Filling

2.1 What is composite resin?

Composite resin is an organic-inorganic complex material, which consists monomer matrix as an organic component, a filler containing glass as an inorganic component as the main component, and a material composed of these interfaces.

A monomer is an organic material with a property of polymerization and conversion into polymer resin. In dental materials in particular, it is often a mixture of crosslinkable (meth) acrylate monomers in many cases. The nature of polymerization, whereby a monomer with flowability becomes a solid polymer, is relevant to important core functions of composite resin. That is, while the monomer has the property that a shape can be given freely before polymerization, it takes on its characteristic function of maintaining shape after polymerization.

Urethane dimethacrylate (UDMA) and triethylene glycol dimethacrylate (TEGDMA), which are employed widely for dental restorations, are shown in Figure 1.
In addition to these, various monomers are used, and a predetermined viscosity and a polymerization shrinkage rate have been fixed by mixing monomers and monomers with different properties.


UDMA

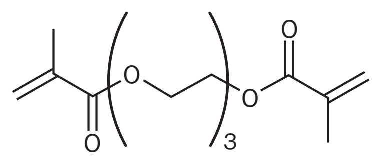
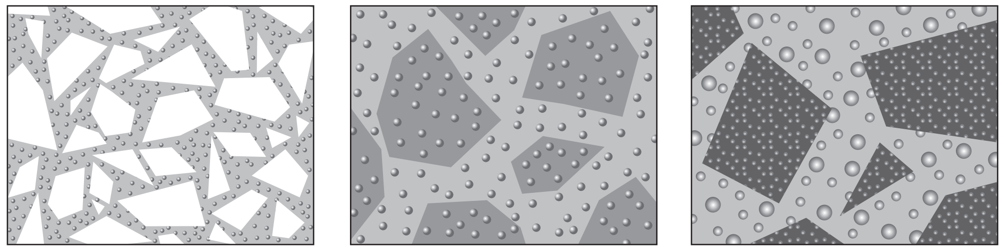

TEGDMA

Figure 1. Monomers employed as dental materials

Particulate alumina or zirconia is used for the inorganic filler, and when it is combinedwith a monomer, it becomes an uncured composite resin. By mixing the fillers, the matrix can be given mechanical properties such as flexural strength and hardness. Fillers used in dental materials include inorganic fillers of submicron to several-micron diameters, nano-sized colloidal silica, and organic composite fillers prepared by mixing monomer in advance with nanofiller and polymerizing them, and then pulverizing them. These fillers have various properties and particle diameters. Changing the components and shapes used for the inorganic filler increases the range of functions such as improvement of abrasiveness and operability, impartation of sustained fluoride release, and the like. Furthermore, the operability of the paste is adjusted by using these fillers in combination (Figure 2).



Amorphous inorganic filler of micron size of 1 to 10 μm, Spherical nano filler of 10-100 nm

Spherical inorganic filler of submicron size of 200-300 nm, Organic complex filler of 20-30 μm containing submicron filler of 200-300 nm

Spherical inorganic filler of micron size of 0.5-1 μm, Organic complex filler of 10-50 μm contain nano filler of 10-30 nm

Figure 2 Image of Fillers being mixed

As shown in the above images, each monomer and inorganic filler plays an important role. However, sufficient strength and durability will not be obtained unless they are firmly combine strongly at the interfaces. This is because destruction occurs at the interface between the matrix and the filler in the event of considering destruction or fracture of the complex material. Many monomers are lipophilic, and the surface of the inorganic filler is hydrophilic, so their affinity is not high. A method used to solve this point is a silane coupling treatment; the inorganic filler subjected to the coupling treatment is modified so as to have a lipophilic surface and to have high affinity with the monomer. As a result, mixing inorganic filler highly is possible, and after polymerizing and curing, it firmly bonds with the polymer matrix, greatly contributing to high strength and high durability of the composite resin.

As described above, in order for the composite resin to satisfy the performance levels required of a dental material, the monomer, the inorganic filler and their interfaces must achieve their respective roles sufficiently.

2.2 Photo-radical polymerization reaction mechanism by photosensitizer

To obtain polymer from monomer, a particular reaction called polymerization reaction is necessary. The polymerization reaction is classified as a chain reaction or a successive reaction. In the chain reaction, as soon as a polymerized active species is formed from the monomer, it reacts with another monomer, followed by a rapid reaction to another monomer. (Figure 3) As a result, the monomer changes instantaneously to a mixture of high molecular weight polymer and unpolymerized monomer by chain reaction. By contrast, since the consumption of the monomer is slow in the successive reaction, it takes some time for the polymer to achieve a high molecular weight.

When the polymerizable group is a monomer (crosslinkable monomer) with a plurality in the molecule, the polymer forms a network structure (crosslinked structure) by polymerization, and as the

polymerization progresses and the density of the polymer network structure increases, and it does not dissolve in solvent of small molecular weight.

In other words, monomer can be cured in an extremely short time by the chain reaction.
Radical polymerization is one of patterns in a chain reaction like this. It provides a wider range of monomers and applicable reaction conditions than other patterns of polymerization reaction.
Radical polymerization is the most appropriate method to instantly cure a dental material containing monomer in the oral cavity under high humidity. This is a polymerization reaction frequently used for dental materials.

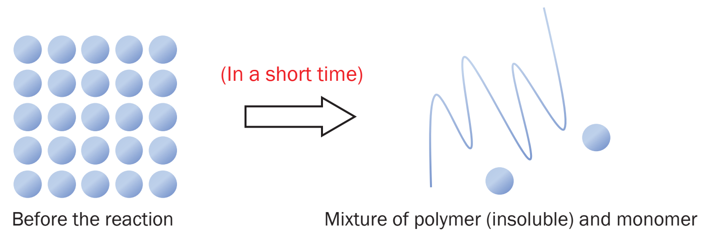


Figure 3 Chain reaction (Radical polymerization)

Since the composite resin is polymerized by irradiation with visible light, the monomer and the photosensitizer are combined. When irradiated with light, radical polymerization of monomers occurs, and polymers are formed and cured.

Radical polymerization usually does not proceed with the monomer alone. A thermal sensitizer in the case of polymerization by heating, and a photosensitizer in the case of polymerization by light irradiation, are used as an initiator. Many of the composite resins are polymerized and cured by light irradiation using a photosensitizer such as camphorquinone (CQ) or a promoter such as tertiary amine.

Radical polymerization is constituted by at least 4 kinds of elementary reactions, initiation, propagation, termination, and chain transfer, shown in Figure 4. In the case of polymerization by light irradiation, the photosensitizer generates an initiating radical by light irradiation; then a propagating radical is generated by addition of the initiating radical to a monomer. These two reactions are the initiation. In propagation, a propagating radical grows to high molecular weight by repeating additions to a monomer one after another. At termination, growth radicals become inactive due to recombination or disproportionation by two molecules of growing radicals, and high molecular chains of one molecule or two molecular are generated.

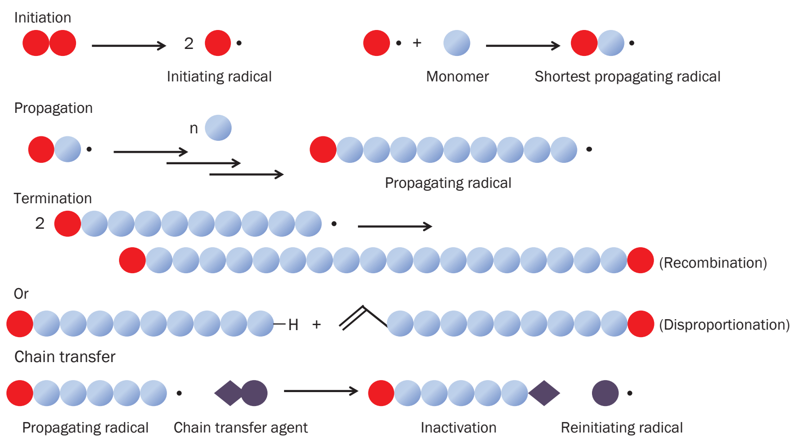


Figure 4 Elementary reactions of radical polymerization

2.3 Initiating reaction and light irradiator

Radical polymerization of composite resin is initiated by light irradiation from a light irradiator, but the light used for initiation has to be absorbed by the photosensitizer.

CQ is widely used as a photopolymerization initiator for dental materials; it shows an absorption maximum around 470 nm and is therefore excited by light irradiation in this wavelength region. Photoexcited CQ withdraws hydrogen from a hydrogen donor such as a tertiary amine and generates an initiating radical. From the CQ/amine type initiator, two types of radicals are generated by visible light irradiation, but CQH does not cause addition to the monomer due to its large solid life. By contrast, R "CH (.) N (R) (R2 ') causes addition to the monomer and becomes an initiating radical.

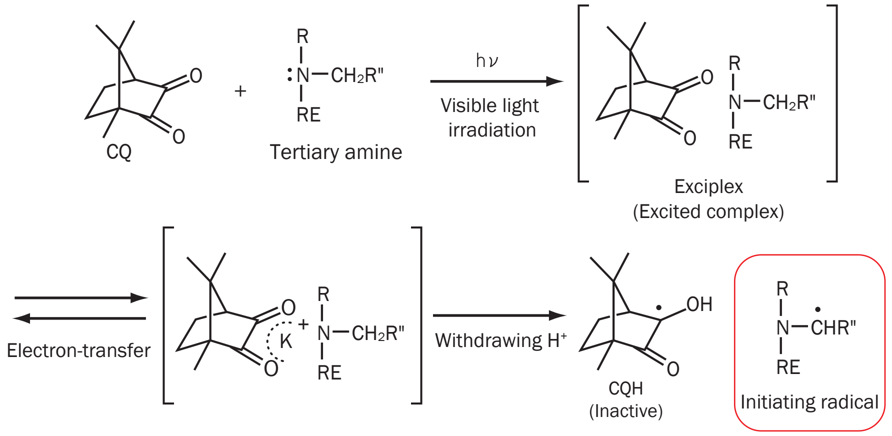


Figure 5 Generating radical from CQ/Tertiary amine initiator by visible light irradiation

In other words, a resin material which is employing CQ as photosensitizer is polymerized and cured by irradiation light whose wavelength is around 470 nm.

Depending on the intensity of the irradiation light, the rate of polymerization and the physical properties of the generated polymer (cured dental material) are different. Light curing material must be irradiated with light of appropriate wavelength and intensity. If it is not appropriate, it is impossible to sufficiently proceed the initiating reaction, and as a result, it is thought that the polymerization may be insufficient, and the material after polymerization may not be able to exert its original physical properties. At present, light irradiators with various light sources and light quantities are commercially available. Halogen lamps, plasma lamps, and LED lamps are used as light sources, but in recent years LED light irradiators have become mainstream (Table 1).

Also, in LED light irradiators, products with the highest maximum irradiance have been made commercially available in order to shorten the curing time of resin materials, and the irradiation time that can be set has also become shorter. Products (Penguin Alpha etc.) which have both blue LED (about 470 nm) and purple LED (about 400 nm) are also on sale so that they can also be applied to surface lubricants and whitening.

Table 1 Commercially available light irradiator

Manufacturer	Product Name	Effective Wavelength Region (nm)	Maximum Emissive Power (mW/cm²)
PIERCE/YAMAKIN	Penguin α	380 ~ 415 440 ~ 480	2400
PIERCE	Delight ortho	420 ~ 490	2700
YOSHIDA	BlueLEX Alpha	450 ~ 470	1400
ULTRADENT JAPAN	VALO curing light	395 ~ 480	4500
	VALO CORDLESS	395 ~ 480	3200
MORITA	PenCure 2000	450 ~ 470	2000
Kerr	Demi Ultra	450 ~ 470	1330
GC	G-Light Prima-II Plus	390 ~ 410 455 ~ 475	2000
Hakusui	mini L.E.D. III	420 ~ 480	3300
Ivoclar Vivadent	Bluephase 20i	385 ~ 515	2200
	Bluephase Style 20i	385 ~ 515	2000
MICRO TECH	LEDEX Turbo WL-090	440 ~ 480	2400
Forest-one	FUSION 5	420 ~ 490	4000
Dental Technica	NOBLESS	430 ~ 490	3000
DENTRADE	D-LUX LED	430 ~ 490	2400
B.S.A sakurai	X Light	430 ~ 480	2500

Each product has various features and it is necessary to irradiate the composite resin to be used with light with the appropriate light amount and time.

The instructions for use, in many cases, when comparing halogen lamps with LED lamps, indicate that LED lamps can shorten the irradiation time to about half. This is because LED lamps can irradiate light of 470 nm, which is the excitation wavelength of CQ, in a limited manner as compared with halogen lamps, and even if the irradiation time is short, a sufficient polymerization rate can be achieved. The development of such a light source also contributes to the efficiency of dental treatment.

2.4 Expanding the scope of applications

For composite resin, flowable type is available. In order to facilitate filling into cavities of different sizes and shapes, each product has unique properties such as very high flowability or the ability to shaped while filling is in progress. Recent technological developments have been remarkable; they include a flowable type with strength which not inferior to that of the universal type, and products showing a curing depth of 4.0 mm by photopolymerization. Composite resin will continue to evolve in the future and it is thought that it will increase its value in restorative treatment.

3. Concept of TMR-Z Fill 10.

3.1 Making full use of filler technology

The resin-based dental restorative material iGOS, released by YAMAKIN in February 2016, realized both strength and sustained fluoride release property, a combination which had been thought difficult to achieve. This technology later helped hybrid resin blocks for CAD/CAM to obtain a competitive advantage.

Now, we have carried the concept of "iGOS" further, and launched a new product, "TMR-Z Fill 10. ("Z Fill"), in pursuit of qualities such as easy operability and outstanding color tones in clinical practice. The key point of this technology is to make full use of YAMAKIN's filler technology.

Table 2 YAMAKIN's filler technology

Image	Filler Technology	Effect	Application to Z Fill	
			Universal	Flow, Low Flow
	Ceramics Cluster Filler (C.C.F.)	Improving mechanical strength	✓	–
	Sustained Fluoride Release Filler	Sustained fluoride release property; recharge of fluoride	✓	✓
	Spherical Nano-Filler	Improving mechanical strength and operability	✓	✓
	Organic and Inorganic Composite Filler (OCF)	Improving operability and aesthetics	✓	✓

As shown in Table 2, various fillers are combined depending on the product concept. These include ceramics cluster fillers (C.C.F.), spherical nano filler of about 20 nm (essential for achieving high strength), sustained fluoride release fillers (for imparting fluoride sustained release property), and organic composite fillers (for improving operability and aesthetics). "Z Fill" can be said to be a culmination of YAMAKIN's use of all of the filler technologies carefully developed in our past resin products.

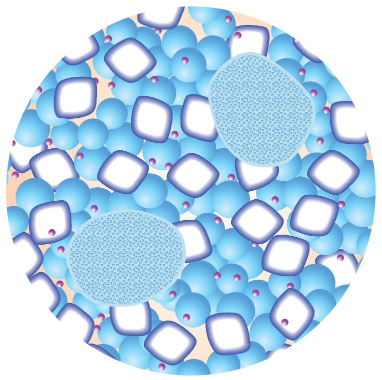


Figure 6 Image of fillers in Z Fill (Universal)

3.2 Innovation through the TMR Series

YAMAKIN's TMR Series consists of "Z Fill," the dental adhesive for dentine, "TMR-AQUA BOND 0" (Figure 7), and the dental pulp capping material "TMR-MTA cement Mielle" (MTA CEMENT). (Figure 8) The series is used for the mission of "no extraction," "minimal grinding," and "preserving teeth" based on the MI concept.

Figure 7 TMR-AQUA BOND 0

For example, pulp protection treatment is an important treatment for preserving natural teeth. However, the success rate is low. To avoid the risk of infection, extraction of pulp is chosen in many cases. To help solve such a process gap, YAMAKIN offers the innovations which we have combined in the functions of TMR series.

Figure 8 TMR-MTA cement Mielle

We will pursue the possibilities of pulp protection through the functions of each product. "MTA CEMENT" exhibits good sealing, excellent stability after curing, and promotion of hard tissue formation, as confirmed in experiments.
"AQUA BOND" (see below for its adhesion concept) adheres to MTA CEMENT, and enables immediate CR filling after the dental pulp protection treatment carried out using "MTA CEMENT". "Z Fill" releases fluoride ions and is expected to strengthen teeth substance and inhibit bacterial adhesion.

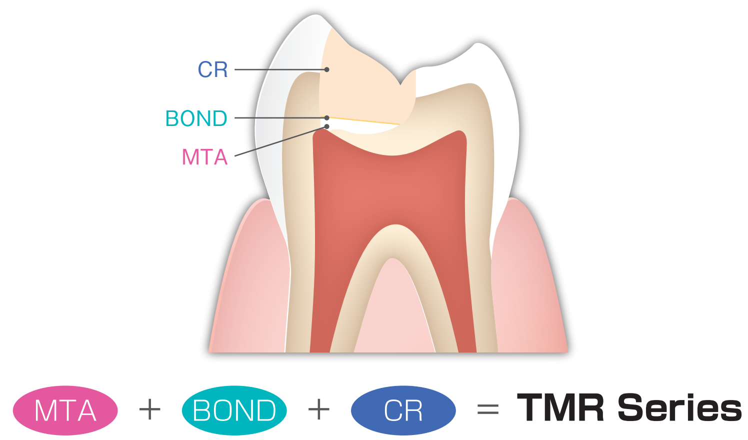


Figure 9 Innovation through the TMR Series

Concept of adhesion of "MTA CEMENT" and "AQUA BOND"

"MTA CEMENT" contains moisture since it is made into a paste by being mixed with water; therefore, it does not combine well with hydrophobic bonding materials. However, "AQUA BOND" is hydrophilic thanks to M-TEG-P®, whose adherent component is amphiphilic; as a result, it combines well with the moisture-containing "MTA CEMENT," and it is thought that it adheres also to irregularities on the cement surface.

It is known that the phosphoric acid monomer reacts excellently with zirconia[1-3]. It is thought that binding between zirconia, which is the radiographic agent for "MTA CEMENT," and the phosphate group of M-TEG-P, which is contained in "AQUA BOND," will be effective for adherence (Figure 11).

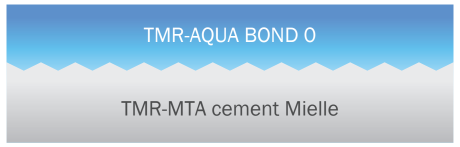


Figure 10 Image of interface

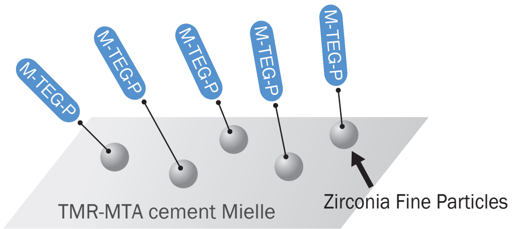


Figure 11 Binding between M-TEG-P and Zirconia

The evaluation results for the bonding strength of the TMR Series, which is a complete system for adhering "Z Fill" to "MTA CEMENT" using "AQUA BOND," are shown in Figure 12.
A silicon mold was filled with "MTA CEMENT" after it had been mixed with water. It was dried by air (0-30 sec) 5 min after mixing. "AQUA BOND" was applied on it, then a stainless bur was set as a test specimen, using resin cement. Tensile bond strength was measured 1 day later.
As shown in Figure 12, a fixed bond strength was confirmed and it can be called a new value for this combination.

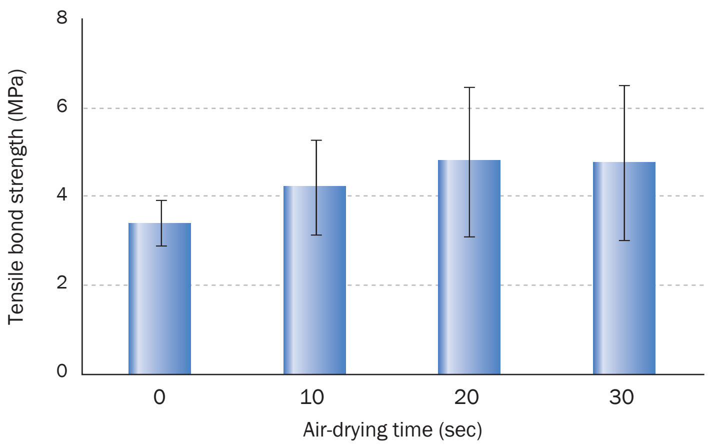


Figure 12 Adhesion by TMR Series

4. Features of "TMR- Z Fill 10."

4.1 Mechanical strength

4.1.1 Flexural strength

Flexural strength of "Z Fill" was evaluated by three-point bending test, with reference to ISO 4049: 2009[4]. To make a test specimen, "Z Fill" was filled ina mold of 2.0 mm×2.0 mm×25 mm, cured by light, and adjusted by waterproof polishing paper. The specimen was kept in a water at 37°C for 1 day, then measured with a small table-top material tester (EZ-Graph: SHIMADZU CORPORATION [Japan]).

For the evaluation of durability, a thermal cycle test is used, which utilizes the difference in coefficient of thermal expansion of constituents and alternately repeats immersion in warm water and cold water to promote deterioration of the material. This test is a model test assuming use in the oral cavity. In this case, conditions of immersing for 30 seconds each at 4°C. and 60°C. were carried out for 5,000 cycles, and then a three-point bending test was conducted to confirm the durability (Figure 13).

The Universal, Flow and Low Flow versions of "Z Fill" showed the same degree of flexural strength and durability; therefore, operators can select the appropriate paste type to be used for the application site without having to consider the strength or durability of each version.

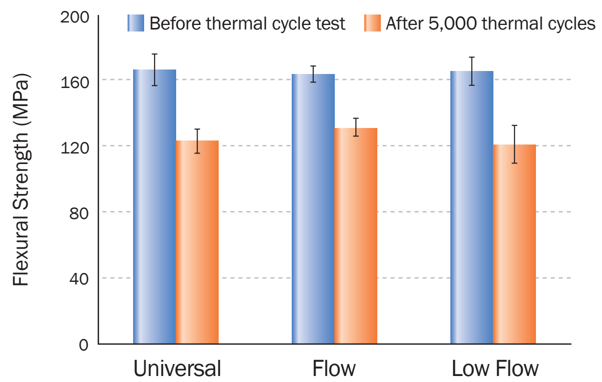


Figure 13 Flexural strength before and after thermal cycle

4.1.2 Vickers hardness

Composite resin need to be cured sufficiently by several seconds of light curing. Therefore, the Vickers hardness of Z Fill was measured by the following method:

"Z Fill" was filled in a mold with a diameter of 12 mm and a thickness of 2.0 mm and irradiated for 10 sec by an LED irradiator with a light amount of 1,000 mW/cm^2 and over. The upper surface (irradiated surface) and the lower surface (non-irradiated surface) of the cured resin were measured with a Vickers hardness tester (HV-113: Mitutoyo) under the conditions of a load of 200 g, a loading time of 15 seconds, and a number of tests of n = 1. The measurement was carried out three times per surface, and the average value thereof was calculated.

The ISO standard [5] of hard resin for dental crowns assumes that the Vickers hardness is 18 (HV 0.2) or more, and that the hardness of the bottom surface is 70% or more of the hardness of the upper surface. The surface of "Z Fill" showed high Vickers hardness and the bottom surface was 70% or more of the upper surface.

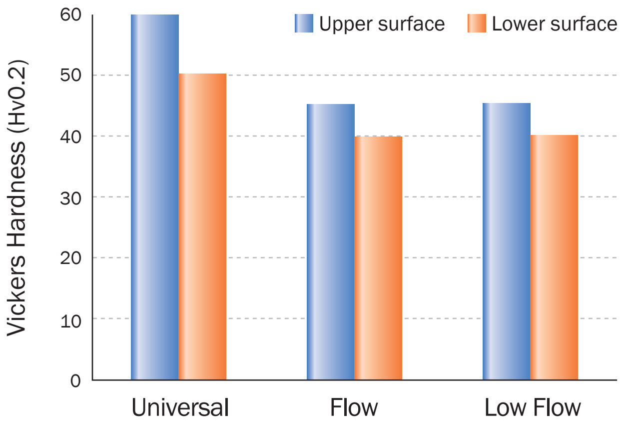


Figure 14 Vickers Hardness

4.2 Operability

4.2.1 Ease of discharge

When conducting restoration by composite resin clinically, it is very important to control the discharge amount from the syringe. Particularly for the flowable type, it is necessary to avoid stress as much as possible when squeezing the product out of the syringe. Therefore, "Z Fill" was designed not only with the contents of the resin but also the shape inside the syringe taken into consideration. It was designed to be able to discharge with less force (about 1/2) than our conventional product, and to be less stringy and easier to control (Figure 15).

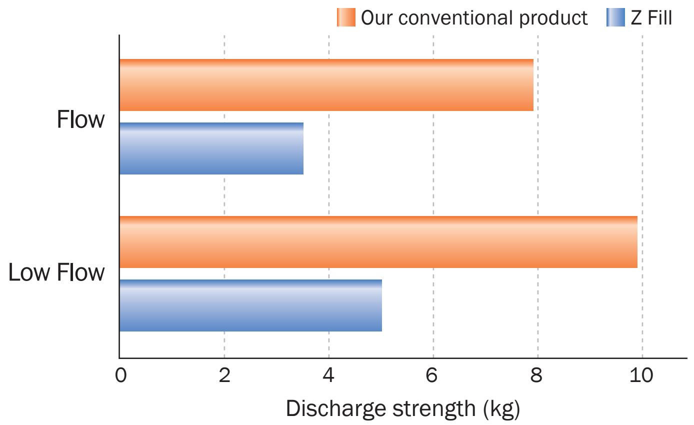


Figure 15 Ease of discharge

4.2.3 Flowability

Two types of flowable type resins with different levels of flowability are available in the "Z Fill" lineup. Using this difference in flowability depending on the case makes it possible to carry out appropriate restoration.

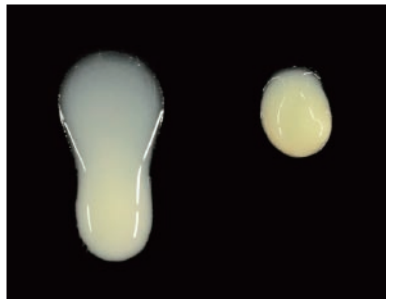


Figure 16 “Z Fill Flowable type”
(Left: Flow, Right: Low Flow)

4.2.4 Formability

"Z Fill universal" has been fine-tuned for consistency, and exhibits minimal entrainment of air bubbles when closely adhering to the tooth substance. Therefore, it is expected that the original physical properties of the product will be demonstrated in clinical practice, too. In addition, while it has the property of adhering to the tooth material, the resin is less likely to adhere to a filling instrument, so separation is favorable. Furthermore, due to its superior formability, delicate repair work is also possible (Figure 17).

Figure 17 Formability of “Z Fill Universal”

For Low Flow, the flowability is designed to be low as described above, and as shown in Figure 18, the shape can be held in the vertical direction. Therefore, it is also possible to restore the occlusal surface using Low Flow.

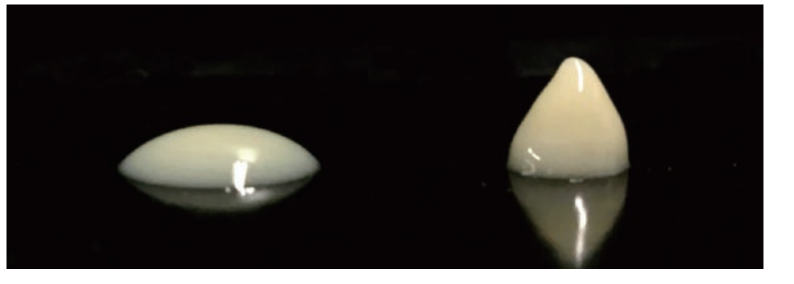


Figure 18 Formability of “Z Fill” Flowable type resin
(Left: Flow Right: Low Flow)

4.2.5 Polishability

It is said that plaque tends to adhere easily unless its surface roughness is made as small as possible by firmly polishing after restoration by composite resin. Since the operation is carried out in the oral cavity, it is required to have characteristics such that polishing is completed in a short time, in order to minimize the burden on the patient as much as possible. Figure 19 shows "Z Fill Flow" polished only with tissue paper. "Z Fill" is designed to be easy to polish and to obtain gloss by deploying filler technology.

Figure 19 “Z Fill Flow” polished by tissue paper

4.3 Color tone

4.3.1 Line-up

Figure 20 shows samples of color tones of "Z Fill" when irradiated for 10 seconds with a light irradiator with a light amount of 1,000 mW/cm^2 or more. Note that each sample has a thickness of 1.0 mm, and the color tone changes depending on the thickness and the background color.

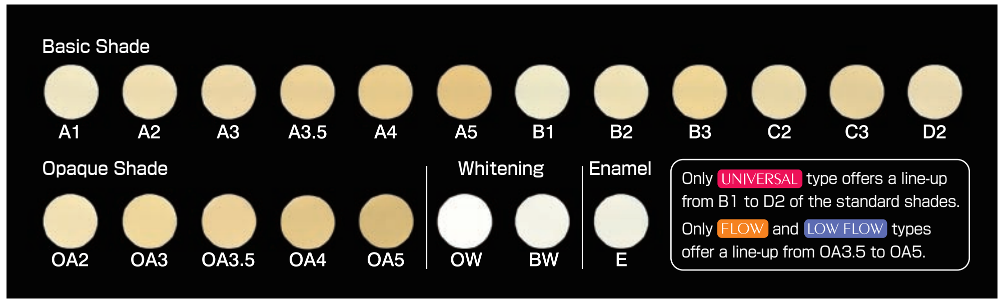


Figure 20 Sample of color tones of "Z Fill"

"Z Fill" is designed to have a high transmittance, and it is possible to naturally reproduce the color tone of the incisal tooth etc. Therefore, it is possible to repair one treatment with one shade. The universal type has 17 colors and the flowable type has 14 colors, so you can choose the appropriate color tone for everyone, regardless of age and case (Table 3).

In addition, A5 and OA5 shades, which are popular in our conventional products, are available in the lineup. These have lower lightness than the A4 shade and they have high color saturation. They are therefore effective for tooth substance with high color tone, such as cervical teeth in the elderly.

Table 3 Line-up

Product name	Category	A1	A2	A3	A3.5	A4	A5	B1	B2	B3	C2	C3	D2	Others	QTY of shade	Contents
Z Fill 10. Universal	Dentine	●	●	●	●	●	●	●	●	●	●	●	●	BW, E, OW	17	3.8 g (2 mL)
	Opaque		●	●												
Z Fill 10. Flow	Dentine	●	●	●	●	●	●							BW, E, OW	14	2.6 g (1.5 mL)
	Opaque		●	●	●	●	●									
Z Fill 10. Low Flow	Dentine	●	●	●	●	●	●							BW, E, OW	14	2.6 g (1.5 mL)
	Opaque		●	●	●	●	●									

BW: Bleaching White E: Enamel OW: Opaque White

4.3.2 Chameleon effect

In combination with the filler technology, excellent light-scattering property was achieved while maintaining the same transmittance as our conventional products. A chameleon effect can be expected from this characteristic, since the light scatters so that the surrounding colors become more natural.

Figure 21 Light-scattering property
(Left: Z Fill Right: Our conventional product)

4.3.3 Coloring resistance test

Given the aesthetics of composite resin restoration, it is also important to evaluate the effect of discoloration and coloring due to food and drink. on this occasion, coloring resistance evaluation of "Z Fill" was carried out using black tea, as follows:

"Z Fill" was filled in a mold with a diameter of 15 mm and a thickness of 1.0 mm, and cured with a light-curing device. The cured surface was then mirror-polished to be used as a test specimen.
Bovine teeth were prepared by exposing dentin and enamel in advance, and placed in the center of a mold with a diameter of 25 mm and a thickness of 1.5 mm. After that, the specimen was held with a resin so that the resin exposed surface became a flat surface, and the specular surface was polished to prepare a test piece. Each test piece was immersed in a black tea aqueous solution and stored in a thermostatic chamber at 37°C, taken out from the container at each immersion time of 6, 24, and 48 hours, and thoroughly washed with running water. After washing, the test specimens were measured with a spectrophotometer (CM-3610d: Konica Minolta) to calculate the color difference ΔE from the test piece before coloring.

As shown in Figure 22, the degree of coloring tends to increase as the immersion time of both the resin material and the bovine teeth increases. However, when comparing bovine teeth with "Z Fill" which was immersed in tea solution for 48 hours, it was confirmed that "Z Fill" was more difficult to color with black tea solution.

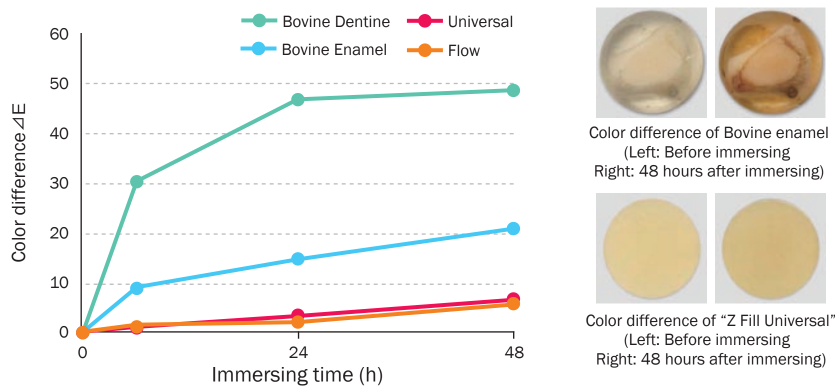


Figure 22 Coloring resistance test (black tea solution)

4.4 Sustained fluoride release property

4.4.1 Amount of released fluoride ions

It is known that fluoride ions taken into the oral cavity exhibit decalcification suppression of enamel, promotion of remineralization and caries prevention effect [6-10]. In anticipation of these effects, "Z Fill" is mixed with sustained fluoride release fillers. Therefore, the sustained fluoride release property of "Z Fill" was evaluated as follows;

"Z Fill" was filled in a mold with a diameter of 12 mm and a thickness of 0.5 mm and cured by a light-curing device. The surface of the cured test specimens were then trimmed with a waterproof abrasive paper. After washing the test specimens thoroughly with running water, they were immersed in 15 ml of distilled water. After a predetermined period of time, the specimens were taken out and the fluoride ion concentration of the immersion water was measured with an ion meter (F-55: Horiba Seisakusho) to calculate the sustained release amount of the fluoride ion per unit area.

The measurement (Figure 23) demonstrated that "Z Fill" stably releases fluoride ions over a long period of 2 months or longer.

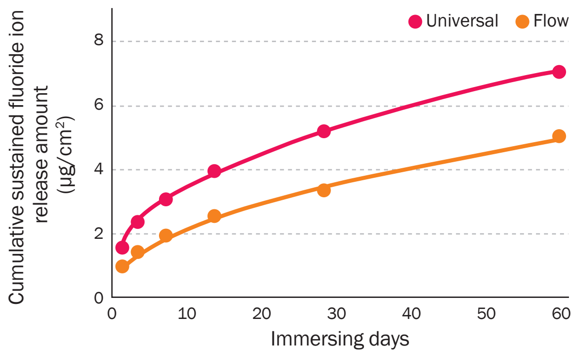


Figure 23 The sustained release amount of fluoride ions

4.4.2 Fluoride recharge property

"Z Fill" was tracked for the amount of sustained release fluoride ions for 2 months, and it is thought that its sustained release amount will decline. However, the fluoride sustained-release fillers used for "Z Fill" can be recharged with fluoride ions by brushing with a toothpaste containing fluoride. The following model experiment was conducted for verification:

"Z Fill" was filled in a mold with a diameter of 12 mm and a thickness of 0.5mm and cured by light-curing device. The surface of the cured test specimens were then trimmed with a waterproof abrasive paper. Test specimens whose fluoride ions were released to certain degree by being totally immersed in 15 ml of distilled water for 48 hours were used. Brushing of specimens after releasing of fluoride ions was carried out using a simple toothbrush abrasion tester with reference to ISO 14569-1 [11]. The specimens were fixed in a toothpaste suspension containing fluoride. The toothbrush was slid 500 times at a load of 2.0 N and a sliding speed of 850 mm/s. The specimens after brushing were thoroughly washed with running water and the amount of fluoride ions gradually released from the specimens was measured with an ion meter. Brushing and measurement of fluoride ions was performed four times in total.

From the measured amount of fluoride ions (Figure 24), it was confirmed that fluoride rechargeability was exhibited by brushing with a fluoride-containing toothpaste. In addition, it is shown that even if the number of times of recharge is repeated, the sustained release amount of fluoride ions is stable and has high reproducibility. That is, if sustained fluoride release fillers which are used as a composite resin are maintained in the oral cavity for several years or more, they can be expected to exhibit permanent sustained fluoride release by periodic brushing.

On the other hand, recharging behavior was not observed even when the same experiment was performed on a resin material which did not contain sustained fluoride release fillers. As a result, it is understood that this property was derived from the sustained fluoride release fillers which are also used for "Z Fill."

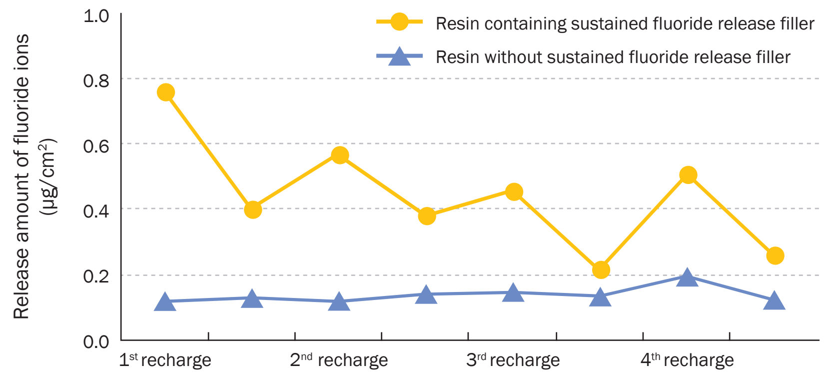


Figure 24 Release amount of fluoride ions when brushing using a fluoride-containing toothpaste

4.4.3 Risks involved in the use of fluoride ions

We have described the sustained fluoride release property of "Z Fill" thus far. Although fluoride has various cariostatic properties, there are some reports about the risks of fluoride.

One example of research on fluoride risks is the investigation about the corrosion of pure titanium or titanium alloys. Since titanium has excellent corrosion resistance and biocompatibility, pure titanium and titanium alloys such as Ti-6Al-4V have been used for dental materials, such as dental implants, denture bases, orthodontics materials. The excellent corrosion resistance of titanium depends on the passive film formed on the titanium surface. However, the passive film may be destroyed by hydrofluoric acid (HF) produced from fluoride under specific conditions [12]. On the basis of the relationship between the corrosion potential and the elution amount of titanium, Nakagawa et al. reported that further corrosion of titanium might easily occur even at low concentrations of fluoride under acidic and low dissolved-oxygen conditions [13-15].

The pH in the oral cavity varies in the range of 4 to 7, due to the ingestion of foods and liquids [16]. Because the proximal surface of the crown restoration, the mucosal surface of the denture base, and the clearance between oral implant superstructures and gingiva are not in contact with the atmosphere, oxygen concentration in these site is 1/3 to 1/10 or less than that of the atmosphere [17].

In the oral site with low pH and low concentration of oxygen, dental materials containing fluoride, such as tooth surface coating agents (about 9,000 ppm), toothpaste (about 900 ppm) or mouthwash (about 450 ppm) may cause the corrosion of titanium. If the corrosion resistance of the titanium or titanium alloy implant body is lowered by the fluoride generated in the oral cavity, there is concern about corrosion and breaking of implants. However, in actual professional care at dental clinics, application of a neutral sodium fluoride solution is recommended, avoiding application of a phosphoric acid acidic sodium fluoride solution. In addition, most fluoride products used in home care are pH neutral. Therefore, it is considered that the application of fluoride containing products in the oral environment does not cause the corrosion of titanium implants.

Through a literature review, Aida et al. acknowledged the possibility that titanium–implants may be slightly corroded by dental materials containing fluoride and used in the oral environment, because titanium may be slightly corroded by fluoride in neutral or mildly acidic conditions of pH 4.7 or lower. However, they presume that the probability of titanium corrosion in the weakly acidic region is extremely low [18]. In addition, it has been reported that the fluoride concentration in saliva after brushing with toothpaste containing fluoride significantly decreases over a short time [19].

As described above, it is considered that the risks involved in the use of fluoride derived from available dental materials for the corrosion of titanium prostheses are minimal. The sustained release amount of fluoride ions for "Z Fill" is 1.4 μg/cm^2 (Universal type) a day, which is much lower than the amount of fluoride contained in tooth surface application agents and in toothpaste. Therefore, it can be presumed that the possibility of corrosion of titanium by the fluoride released from "Z Fill" is minimal.

4.5 Biological safety

The biological safety of medical devices which come into contact with the human body must be evaluated. Biological safety issues include cytotoxicity, irritation, sensitization, genetic toxicity, implantation and so on. Appropriate tests are conducted on the basis of the nature of the physical contact and of the contact duration of the medical devices taking the characteristics of the medical devices into consideration.

This section describes the cytotoxicity test of "Z Fill" using the human monocytic leukemia cell line THP.1 cell (distributed by the Department of Oral and Maxillofacial Surgery, Kochi Medical School, Kochi University) (Figure 25).

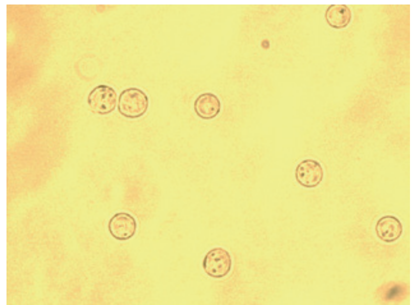


Figure 25 Human monocytic leukemia cell line THP.1 cell

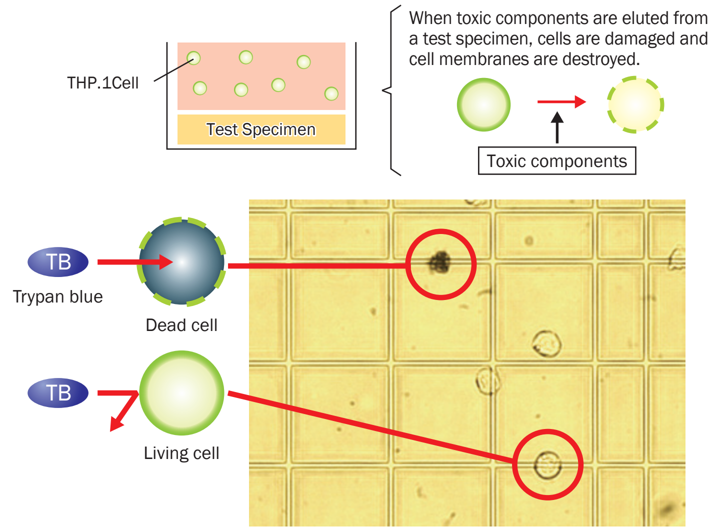
〈Test Specimen〉

Each type of “Z Fill”—Universal, Flow, and Low Flow—was filled in a mold with a diameter of 15 mm and a thickness of 1.0 mm and cured by light-curing device. The cured test specimen was then polished with a waterproof abrasive paper (P2000) and placed in a well of 24-well plate. 100,000 THP.1cells were seeded on the specimen and cultured at 37°C for 3 days under 5% CO_2. Cells cultured without test specimen were used as a control.

4.5.1 Trypan blue-exclusion test [20]

When cells are cultured on test specimens with toxicity, toxic components are eluted from the test specimen into the cell culture medium. When cells are damaged by toxic components, the cell membrane that separates the interior of the cell from the outside environment is destroyed. Because the cell membrane can exclude dyes such as trypan blue, in the mixture of cell suspension and trypan blue, living cells have a clear cytoplasm whereas dead cells have blue cytoplasm stained with trypan blue. Therefore, counting the number of clear cells (living cells) and blue-stained cells (dead cells) (that is, the proportion of living cells in cultured cells) with a hematocytometer allows evaluation of the effect of the specimen on cell viability (Figure 26).

As shown in Figure 27, all types (Universal, Flow, and Low Flow) of "Z Fill" had high cell viability equivalent to that of the control.



Trypan blue are taken up to the cell with destroyed cell membrane, and stains the cytoplasm.

Figure 26 Principle of Trypan-blue exclusion test

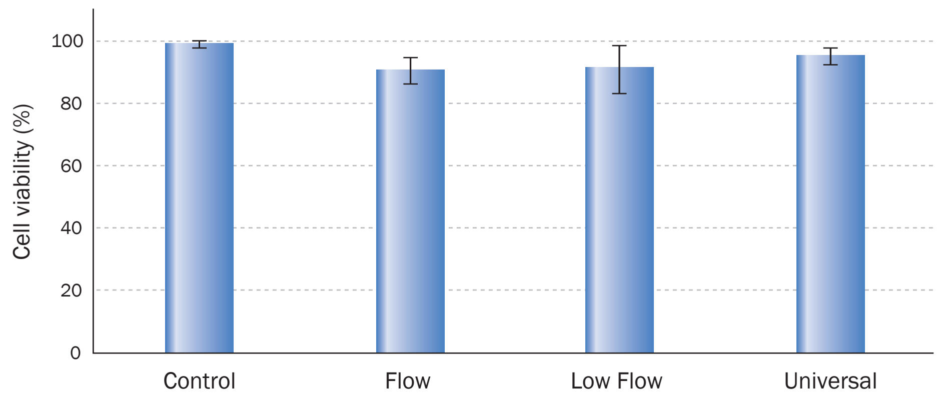


Figure 27 Cell viability of THP. 1 Cell

4.5.2 WST-8 Cytotoxicity test [21, 22]

WST-8 (2-(2-methoxy-4-nitrophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfophenyl)-2H-tetrazolium) is reduced to the orange-colored WST-8 formazan (λmax = 450 nm) by dehydrogenase contained in living cells. On the basis of this principle, quantification of WST-8 formazan measuring absorbance at 450 nm can evaluate the metabolic activity of the cell cultured on test specimen. That is, in the cells cultured on the cytotoxic specimen, the absorbance at 450 nm is low (light orange), whereas in the cells cultured on the non-cytotoxic specimen, the absorbance at 450 nm is high (dark orange) as shown in Figure 28.

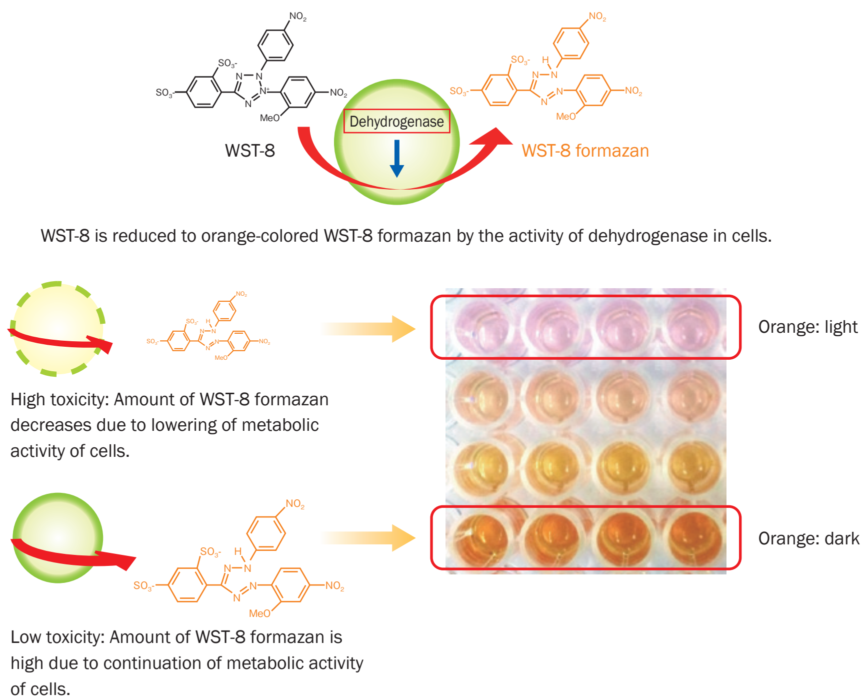


Figure 28 Principle of WST-8 Cytotoxicity test

Cells cultured on a test specimen were transferred to wells of 96-well culture plate, and WST-8 reagent was then added to the wells. After incubation at 37°C for 2 hours, the absorbance of WST-8 formazan was measured at 450 nm. In "Z Fill" (Universal, Flow, Low Flow), all test specimens showed equivalent absorbance to that of the control, and no adverse effect of "Z Fill" on the metabolic activity of THP.1 cells was observed (Figure 29).

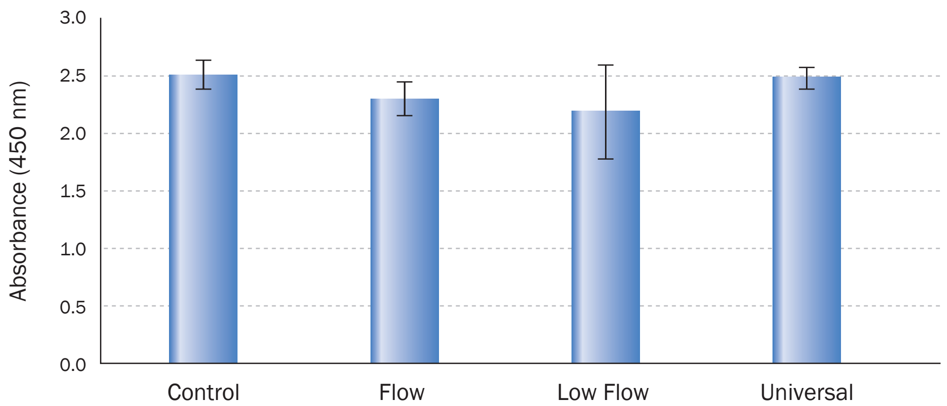
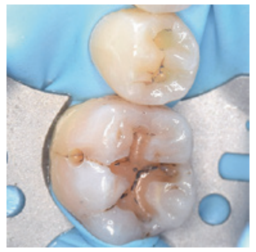


Figure 29 Metabolic activity of THP.1 cells

5. Clinical Cases

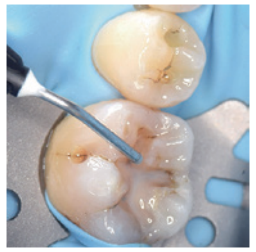
The following clinical cases do not include the entire composite resin restoration process. Please check the instructions for use for details of actual use and for operational methods.

■ Case 1, Repairing cavity (Photo provided by: Yamakita Dental Office (Kochi, Japan))

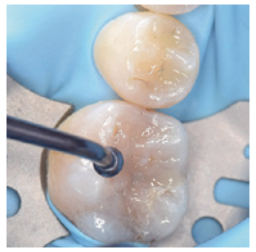


1. Forming a cavity

2. Applying AQUA BOND



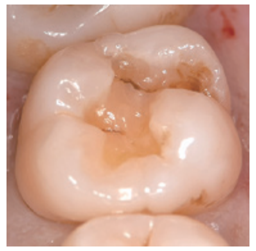
3. Filling with Z Fill Flow



4. Filling with Z Fill Universal

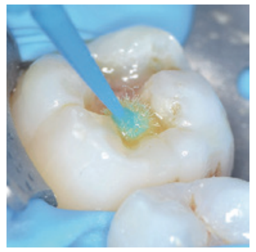
5. After the treatment

■ Case 2, Repairing cavity (Photo provided by: Yamakita Dental Office (Kochi, Japan))



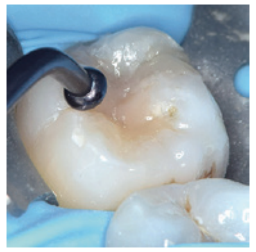
1. Forming a cavity

2. Applying Multi-Echant



3. Applying AQUA BOND

4. Filling with Z Fill Flow



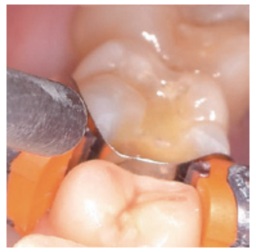
5. Filling with Z Fill Universal

6. After the treatment

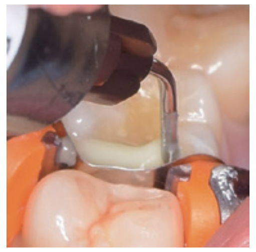
■ Case 3, Repairing cavity (Photo provided by: Yamakita Dental Office (Kochi, Japan))


1. Forming a cavity


2. Applying AQUA BOND


3. Air drying


4. LED light irradiation


5. Filling with Z Fill Flow


6. Filling with Z Fill Universal


7. After LED light irradiation


8. After the treatment

6. Conclusion

Through its process of research and development, YAMAKIN has created "iGOS"—a composite resin for dental filling which combines the features of "strength" and "sustained fluoride release property," a combination which had been thought difficult to achieve. Through this advancing technology, we have launched a new product, "TMR-Z Fill 10.," with characteristics which include excellent clinical handleability and color tones in addition to the advantages of "iGOS." This product is a dental material that fully utilize the YAMAKIN's filler technology.

We hope to improve patients' quality of life by the application of this product in dental treatment based on the MI concept of preservation of as much of the natural tooth structure as possible. We also would like to continue to create new products and services needed by our customers.

The joint research group of YAMAKIN and Kochi University conducted experiments in the cytotoxicity test.

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iGOS
Controlled Medical Device- Resin-based Dental Restorative Material

KZR-CAD HR Block 2
Controlled Medical Device - Resin Material for Dental Milling and Machining CAD/CAM Material for Dental Material

KZR-CAD HR Block 3 GAMMATHETA
Controlled Medical Device - Resin Material for Dental Milling and Machining CAD/CAM Material for Molars

TWiNY
Controlled Medical Device -Composite Resin for Crowns and Bridges

Luna-Wing
Controlled Medical Device -Composite Resin for Crowns and Bridges

Lineup

TMR Z Fill 10. TMR-Z Fill 10.

Controlled medical device -Resin-based Dental Restorative Material

Single Package	TMR-Z Fill10. Universal 3.8g (2mL)
Single Package	TMR-Z Fill10. Flow 2.6g (1.5mL) Accessory. Needle Tip: 10 pcs.
Single Package	TMR-Z Fill10. Low Flow 2.6g (1.5mL) Accessory. Needle Tip: 10 pcs.

Set Package

Standard Pack (each 1 of A1, A2, A3, E)

- Universal
- Flow
- Low Flow

A1x1, A2x1, A3x1, Enamelx1

2 pcs Pack (each 1 of A2, A3)

- Universal
- Flow
- Low Flow

A2x1, A3x1

3 pcs of Same Shade Pack (Each 3pcs.of A2, A3, A3.5)

・Universal	A2x3
・Flow	A3x3
・Low Flow	A3.5x3

Accessory	Needle Tip: 20 pcs.

Related Products

TMR AQUA BOND 0

Controlled medical device
- Dental Adhesive for Enamel and Dentine (Dental adhesive for ceramics) (Dental adhesive for metal)

Single Package	TMR-AQUA BOND 0 (5mL)
Set Package	TMR-AQUA BOND 0 Set ・TMR-AQUA BOND 0 (5mL) : 1pc. ・Disposable Applicator Brush : 50 pcs. ・Disposable Plate : 25 pcs.
Set Package	2 pcs Pack of TMR-AQUA BOND 0 ・TMR-AQUA BOND 0 (5mL) : 2pcs.
Accessory	Disposable Applicator Brush : 50 pcs. Disposable Plate : 50 pcs.

TMR MTA cement Mielle

Controlled medical device - Dental pulp capping material

Single Package

TMR-MTA cement Mielle (White, Light Ivory)
・Microtube Type (0.2g) : 3 pcs.

TMR-MTA cement Mielle (White, Light Ivory)
・Glass Container / Bottle Type (3g)
・Accessory: Spoon (1 pc.)

TMR-MTA cement Mielle (White, Light Ivory)
・Glass Container / Bottle Type (10g)
・Accessory: Spoon (1 pc.)

Multi Etchant

Controlled medical device
-Dental etching material (Adhesive material for dental ceramics)

Multi-use Etchant for
Various Types of Materials and Tooth

Single Package	Multi Etchant (2mL) Accessory : Needle tip 5 pcs.
Accessory	Needle tips for Multi Etchant : 10 pcs.

Multi Primer LIQUID

Controlled medical device
- Bonding material for dental metal (dental ceramics, dental resin)

For intraoral repair of restorations
(metal, ceramics and resin)

Single Package	Multi Primer LIQUID (7mL)

M-TEG-P is a registered trademark of YAMAKIN CO., LTD.

The actual color of the product, model and package may differ from the photographs due to printing ink and shooting conditions.

Manufactured by
YAMAKIN CO., LTD. 1090-3 Otani, Kamibun, Kagami-cho, Konan-shi, Kochi, 781-5451 Japan

We will continue to create value for the future.

Clean room in the YAMAKIN Kochi factory

All manufacturing processes are conducted in clean rooms and controlled extremely strictly.

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