Research Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2016, Volume 4, Issue10
ISSN: 2321–3647(online)

Bleaching of natural dentition: what the new dentist should know

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ABSTRACT

Vital tooth bleaching is a widespread and conservative treatment for the majority of superficial extrinsic or intrinsic stains, compared to composite resin and porcelain veneers, metal and all ceramic crowns. It refers to a process that changes the tooth color without the use of restorative materials. It is a technique of proven safety, as long as certain prerequisites are met by both dentist and patient. Nowadays, a worldwide increase in the desire for whiter teeth is recorded. As part of this increased demand, tooth bleaching is usually incorporated or at least proposed in almost every therapeutic plan, at least for the anterior dental region, under the scope of minimal invasive dental procedures. In vitro and in vivo studies propose different protocols for at-home and in-office bleaching, discussing different degrees of color change and affectivity of the current bleaching products. The aim of this paper is the collection of contemporary evidence-based data concerning tooth bleaching, focusing especially on materials and techniques. Furthermore suggestions on the interpretation of the relevant research data are given. Finally, contemporary evidence-based bleaching protocols based on current bibliography are described.

Keywords: Tooth bleaching, peroxides, OTC products, at-home, in-office protocols

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Received 08 September 2016, Accepted 21September 2016

Please cite this article as: Antoniadou M *et al*., Bleaching of natural dentition: what the new dentist should know. American Journal of Pharmacy & Health Research 2016.

INTRODUCTION

Tooth bleaching is the most conservative treatment for the majority of dyschromias and superficial staining, compared to resin and/or porcelain veneers, metal-ceramic and all ceramic crowns [1]. Today, bleaching is commonly accepted as an absolutely safe therapeutic process, widespread having significant bibliographic documentation [2]. Indeed the number of people seeking improvement of their smile through tooth bleaching, increase rapidly [3]. Dental bleaching refers to any process that changes the tooth color without the use of restorative materials. It can be performed using products available at the dental office (at-home supervised or in-office bleaching) or in pharmacies and e-shops (Over The Counter products- OTCs) [3]. The aim of this paper is the collection of contemporary evidence-based data, concerning tooth bleaching, especially focusing on materials and techniques and the description of certain protocols for effective tooth bleaching.

HISTORICAL OVERVIEW

Tooth bleaching begins in 1848, with Dwinelle, who first described the bleaching process of discolored, non-living teeth, using calcium chloride [2] (Table 1). References were followed by Howell in 1880. In 1961, Spasser described the "walking bleaching technique", which involved placing within the pulp cavity, a mixture of sodium perborate and water [4]. This technique was modified later by the addition of 30-35% hydrogen peroxide, in place of water, in order to maximize the whitening effect. The observation that carbamide peroxide may have a "whitening" effect on teeth was unexpectedly made by the orthodontist Klusmier G., who examined the effect of Gly-Oxid (Marion), which his young patients used during the night in a removable appliance. He discovered that the teeth had become brighter and that lighter tetracycline discolorations had disappeared. He then presented his observations between 1970 and 1975 at different “table clinic” meetings. The periodontist Wagner, a colleague of Klusmier’s, explored the use of the method in adults and subsequently discovered that the gingival was somewhat less inflamed while at the same time the teeth appeared whiter. Slowly the method spread and was adopted in 1988, by Haywood at the University of North Carolina. Haywood and Haymann in 1989, more than 20 years later, developed a home bleaching technique that is still the currently used bleaching procedure [4]. In their article there was an extensive analysis of their technique for bleaching living teeth at-home using custom-made trays and 10% carbamide peroxide solution [5]. This technique had received great acceptance among clinicians and continues in our days to be the most popular [2].

Since then, a number of articles were published on this technique, resulting in greater acceptance and improvement [5-8]. In its current form, this technique involves the use of custom-made trays, placed in the patient's mouth for a few hours per day (or during sleep). No preparation of the teeth (e.g. by an etchant factor) is necessary. Also, there is no need of powerful whitening agents, as the dentist supervises the procedure while the patient performs it alone at his house [2].

Table 1: The most important milestones in the history of bleaching

Year	Authors	Materials	Vital teeth(+) Endodontically treated (-)
1848	Dwinelle	Calcium chloride	-
1868	Latimer	Oxalic acid	+
1877	Chapple	Oxalic acid	+
1879	Taft &Atkinson	Calcium Hypochlorite / Sodium	
1884	Harlan	Hydrogen peroxide	
1910	Prins	Hydrogen peroxide 30%	+,-
1916	Kaine	Hydrochloric acid	+
1918	Abbot	Hydrogen peroxide + heat	
1937	Ames	Hydrogen peroxide 100% + ether 5: 1	+
1942	Younger	Hydrogen peroxide 30% + ether 5: 1	
1984	Harlan	Hydrogen peroxide	
1924	Prins	Hydrogen peroxide + sodium perborate	
1958	Pearson	Hydrogen peroxide	-
1961	Spasser	Sodium perborate + water	-
1967	Nutting &Poe	Hydrogen peroxide 30% + sodium perborate	-
1984	Zaragoza	Hydrogen peroxide 70% + heat	+
1984	McCloskey	Hydrochloric acid	+
1987	Mathenson	Hydrochloric acid	+
1988	Haynie & Emet	Hydrogen peroxide + silicon dioxide	+
1989	Haywood & Heymann	Carbamide Peroxide 10%	+
1991	Jordan	Hydrogen peroxide + halogen lamp	+
1991	Garber & Goldstein	In-office: hydrogen peroxide + light At-home: carbamide peroxide in guard	+
2010	EU	Sodium perborate and boric acid banned	-
2011	EU	0,1-6% hydroxide peroxide only to be sold by dentists	+
2015	CED	Recommendation for prohibition of use of bleaching devices	+, -

MECHANISM OF TOOTH BLEACHING

Bleaching is a complex chemical process. The exact mechanism taking place is yet unknown. It seems that bleaching agents penetrate into the dental tissues and get incorporated. It is believed that the bleaching effect on hard dental tissues differs among the various types of discoloration. Generally, this mechanism involves oxidation reactions where oxygen is released for final

dissolution of the pigments. The dischromatic molecules, such as carotene, have high molecular weight and contain many double bonds (Figure 1). Bleaching agents affect these bonds. The molecules are finally dissolved when their polarity has been changed. Also, changes in the length or shape of these heavy molecules, cause changes in color.

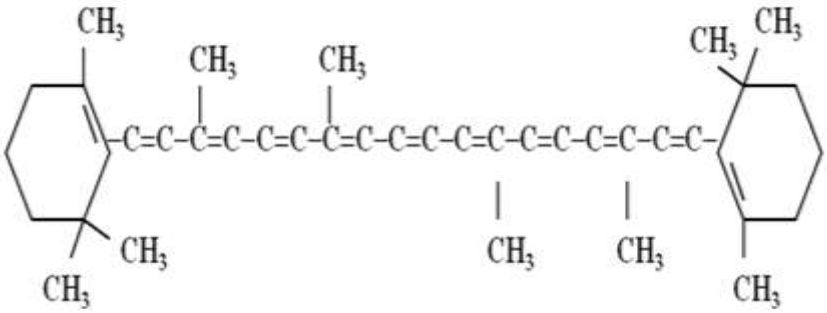

Figure 1: **Beaching agents affect the double carbon bonds as shown on the chemical type of the molecule of carotene.**

Contemporary data argue that dental bleaching is a dynamic process which includes not only minor modifications of the tooth's surface but also of the interior dental tissues, modifications which finally affect their optical properties. The interaction seems not to be limited only to chromophore molecules but is a process that affects healthy enamel too. [6]

The oxidation reactions of the double bonds are conducted by free oxygen radicals. In dentistry, sources of free oxygen radicals are the peroxides:

-Hydrogen peroxide (HP): H_2O_2

-Carbamide peroxide or urea peroxide (CP): $CH_4N_2O \bullet H_2O_2$

As already mentioned, although the precise mechanism of HP oxidation is not entirely clarified, it is believed that free oxygen radicals (O^+) and hydroxyl (OH^{2+}), produced during this reaction, are unstable. Therefore they react with the organic molecules of the dental substitute giving free electrons and resulting in new radicals' formation. These radicals react with the dischromatic molecules, resulting in the formation of new molecules with different optical properties [9]. Among the oxygen (O^+) and hydroxyl (OH^{2+}) radicals, the former has weaker whitening effect, whereas the latter is the most active. At basic pH a greater amount of the hydroxyl free radicals (OH^{2+}) is produced, making the bleaching agent more effective.

The CP is a derivative of the carbonic acid and acts as a mild oxidizing agent. Its solutions are unstable and decompose in saliva and oral liquids into HP (active bleaching agent) and urea (moderate antiseptic action). The generated urea then decomposes into ammonia and carbon dioxide. Ammonia contributes to the rise of pH, as it is a strong base. This step affects the

development of the reaction positively. Finally, HP (from the first reaction) is decomposed because of the unstable nature of the oxygen. A bleaching product with 10% CP gives 3.35% HP and 6.65% urea [2].

BLEACHING MATERIALS

The first bleaching materials were released into public use in the late '80s. Since then, three generations of such materials have been presented. The materials of the first-generation were available in liquid form. Their low viscosity was the cause of difficulties in their use. They were not capable of staying in trays for a long time and therefore a frequent replenishment of the material was required. A lot of side effects were also reported because of that. The materials of the second generation had lower viscosity. They were released in various concentrations of peroxides. Changes in viscosity resulted in a more comfortable use and less irritation of the soft tissues. Finally, third generation materials were launched with differences in excipients and color. Improvements concern both the effectiveness and the limitation of possible side effects.

Recently, the European Union with a respective guideline, regulated the current regime concerning the availability and use of bleaching materials. Specifically, the European guideline 2011/84/EU, which was published the 18th of November 2011 and in force since the 31st of October 2012 in the member-states, regulates the use of HP and other compounds or mixtures which release HP, in bleaching products. This guideline establishes a new legal framework: Bleaching products containing 0.1 to 6% HP can only be sold by/to professionals and their first use should be performed in-office. The rest of the bleaching products can be used by the patients, as long as the access to these products is controlled by the dentist. Additionally, tooth bleaching is prohibited in children and adolescents, under the age of 18 years, except for treatments in-office and only in special cases [10, 11].

The new guideline aims to ensure that only dentists (no other professional group) will have direct access to dental bleaching products containing more than 0.1% and up to 6% HP. These products cannot be directly available to consumers or other professionals. It is noted that 16.62% CP is equivalent to 6% HP. In conclusion, according to this guideline, all bleaching agents that have concentration above 16.62% CP are banned.

- ***Hydrogen peroxide (HP), (H_2O_2)***

HP is the most common active bleaching agent. A variety of HP products, with concentrations that range from 1.5 to 35%, are commercially available. As mentioned above, products with HP concentration above 6%, are for use only in-office. The available products have often a medium viscosity (gel) and contain ingredients for the prevention and treatment of hypersensitivity, as

well as for the improvement of the texture, taste etc. The storage and use of these products must be based on the manufacturer's instructions (for example storage away from the direct sunlight, with low temperature etc.). Depending on the recommended technique products of HP can be used with the assistance of heat, light energy, laser radiation etc.

- ***Carbamide peroxide (CP), ($CH_6N_2O_3$)***

CP is commercially available as a bleaching agent in a gel form and at concentrations of 10 to 35%. As mentioned above, all bleaching agents that have concentration above 16.62% are banned. Generally, these solutions are unstable. In contact with the oral fluids solutions are decomposed into HP and urea. The concentration of 10% CP for use at-home with a custom-made tray is the most common technique and is considered the "gold standard". As already mentioned, a solution of 10% CP gives 3.35% HP and 6.65% urea. Similarly, a solution of 15% CP gives 5.4% HP solution and 9.6% urea.

- ***Sodium Perborate (SP), ($2\ NaBO_2\ (OH)_2\ [H_2O_2]_n$)***

SP is a white, odorless and water soluble chemical compound. It forms crystals as (n) monohydrated ($NaBO_3 \bullet H_2O$), trihydrated ($NaBO_3 \bullet 3H_2O$) and tetrahydrated ($NaBO_3 \bullet 4H_2O$). According to manufacturers, in products containing SP, HP is never included nor is produced after exposure to the oral environment. Therefore there are no HP-derived side effects in the oral cavity. These claims are being investigated, since it is known that the unstable SP decomposes to HP [9].

However, the Council of European Dentists notes that the use of products with boric acid poses risks [12]. It encourages the national associations of member-states to take initiatives to certify that these carcinogenic products will be neither used for tooth bleaching nor placed on the market. So SP and boric acid are forbidden substances for cosmetic products based on the European Union's legislation, without any exception. These chemical substances have been classified as carcinogenic, mutagenic or toxic for reproduction (CMR) and belong to the category 1B of the regulation (EC) 790/2009, which amended the regulation 1272/2008, concerning the classification, labeling and packaging of such substances and mixtures (CLP). They are included in Part 3, Annex VI, of the CLP regulation. This classification applies since the 1st of December 2010.

If a chemical compound is classified as CMR 1B, regardless of its concentration, its use is totally prohibited in cosmetic products (cosmetic products-Article 15 of Regulation Aesthetics-Cosmetics Regulation 1223/2009 [2]). It is a direct prohibition for which no implementation/application measures are necessary. Exceptions can be made if the conditions listed in Article 15 of

Regulation Aesthetics [2], are met. However, since the conditions for the use of these chemical compounds in beauty products are not fulfilled, the SP and boric acid are considered banned in the EU since the 1st of December 2010.

BLEACHING OF VITAL TEETH – TECHNIQUES

- ***At-home bleaching***

At-home bleaching is widely used. The improvement of tooth color is achieved by using mild bleaching agents (10-16% CP). As mentioned above, the patient uses custom-made trays, placed in his mouth with the material within, for a few hours daily (or during sleep at night). This technique was widely accepted due to the article of Haywood and Heymann [5]. In the present article, it is described step by step at the section "Bleaching protocols". The delayed bleaching results in some cases and the patients' demands for more direct and "impressive" color changes have forced the clinicians to search for more effective techniques.

- ***In-office bleaching***

A range of techniques, devices and bleaching materials have been proposed over time for in-office use. The basic in-office bleaching technique is the direct placement of 35% HP in the labial surfaces of the teeth after properly isolating the working field and the gums. The most common application protocol includes 2-4 in-office appointments, in which the material is applied two or three times, for 15 minutes each time, per session. More information on the in-office technique is to be found in the section "Recommended combined bleaching protocol."

Another way of applying the in-office bleaching agents involves the use of special bleaching devices (for example led, plasma, laser, etc.). This technique is based on the basic reactions of the decomposition of HP, in which the effect of light or heat accelerate its decomposition rate. Therefore, the use of a light or heat emission device, simultaneously with the application of the bleaching agent, should be advantageous. But in bibliography, a limited number of studies have shown that their use, in combination with the bleaching agent is more effective than their single use [13]. Tavares et al.[14] showed that the activation of the process with a bleaching device, improved the whitening result by 1.93 shades (Vita shade guide). Ontiveros et al.[15] argued that tooth bleaching enforced with a halogen lamp is more efficient. Finally, Thorse et al.[16] enumerate clearly, the indications and contraindications of bleaching in-office with bleaching devices. However, in a number of following studies, it was found that activation by light or heat does not enhance the result of bleaching in a statistically significant way [17-19]. On the contrary, there is evidence suggesting that in absence of HP, there is not any whitening effect and that the temperature rise which is caused by the devices may be associated with an increased number of

hypersensitivity cases after their application [20,21]. In May 2015, the Council of European Dentists (CED) published a report on the use of bleaching devices (CED-DOC-2015-037-FIN-E).[22] In this report, advices are given for: a) the general population: bleaching devices have not any proven advantage, but instead they may increase the temperature of the teeth [23] resulting in unwanted reactions [24,25]. More specifically, the temperature rise, that occurs temporarily, dehydrates teeth giving the "illusion" of whitening which however soon disappears [26-28]. Additionally, there is a high risk of irritation and burns in gums and overheating of the tooth pulp which can lead to loss of its vitality, b) the dentists: contemporary data do not support the use of bleaching devices. Since similar results can be achieved with less aggressive methods [29] and taking into account the principle of "*primum non nocere*" ("the first thing is to do no harm"), dentists are recommended to abstain from using them [30].

- ***Combined bleaching technique (at-home and in-office)***

The combined bleaching technique (at-home and in-office) gives promising results [31-33]. More specifically, at the studies of Kugel et al.[32], Papathanassiou et al.[33] and Dawson et al.[37], participants who followed the combined protocol showed statistically significant whiter teeth shades, than those who were bleached at-home. Nevertheless, these studies have some drawbacks. The evaluation time of the bleaching effect tends to be small [38], while studies identifying the color for longer periods, for example 2-3 months after bleaching, are rare. Another common drawback is the size of the sample in most surveys. The sample is usually sufficient for in *in vitro* studies, while quite insufficient for *in vivo* ones. So no safe conclusions can be derived. Finally, the method of identifying color and its changes does not follow a widely accepted protocol. This leads to difficult or even inappropriate comparisons between different studies [39].

- ***Bleaching with OTC products (Over-The-Counter bleaching products)***

OTCs are products that can be used by the patient himself at-home, without the guidance of a dentist. Specifically, in the late 90s, cheap bleaching products were launched on the market and since then anyone can purchase them from pharmacies or e-shops. These products contain HP or CP in concentrations, which sometimes are similar to those of products given by the dentist for at-home supervised bleaching. An additional bleaching agent commonly used in such products is sodium hypochlorite (SY) ($NaClO_2$) in combination with an acid as an activator. The SY releases small amounts of chlorine dioxide (ClO_2) in presence of acid, so this compound has whitening effect too [3]. These products are mainly in the form of toothpastes, mouthwashes, adhesive tapes and varnishes.

Toothpastes

They represent more than 50% of the OTC products and rarely contain peroxides in their composition. Their ability to remove pigments is based mainly on the presence of abrasive substances (aluminum oxide, calcium hydrogen phosphate, silicon) in their composition, which remove only superficial pigments. A limited number of studies have examined the effect of different types of whitening toothpaste. It has been shown that they are advantageous in comparison with conventional toothpastes to the removal of superficial pigments only, while their bleaching action is disputed [19,40]. In a recent study, Forner et al.[41] evaluated the effectiveness of a new toothpaste, which enhances enzymatically the CP's (low concentration) action. The results were very encouraging with an average ΔE* change of 5.14 (both in upper and lower anterior teeth). Furthermore, in an article of Joiner et al.[42] the aim was to study the effectiveness of pigments' removal using this particular whitening toothpaste and its effect on enamel and dentin. This double-blind study reported that with this toothpaste, it is statistically more effective the in vivo removal of extrinsic pigments compared to the non-whitening one. Also, the study concluded that there was no clinically significant wear of the enamel or dentin of the bleached teeth due to the enhanced bleaching action, compared to the control group. Furthermore, in a randomized clinical study [43], the efficacy of two whitening toothpastes and a varnish was compared to the application of at-home use with custom-made trays and 10% CP. The results showed that the 10% CP revealed the best visibly assessed results, compared to the other two techniques. Also, the non-pharmaceutical toothpaste was more effective than the pharmaceutical one, but both had better results than the varnish. In that case it was mentioned by the authors that since there was a wide range of whitening compounds in the OTC products of the study, it was very challenging to identify which of them made the whitening difference. Nevertheless, it is generally a fact, that the contemporary products have a polishing, abrasive and superficial function.

Mouthwashes

Mouthwashes are a relatively new category of OTC products, whose potential of preventing stains' incorporation to the teeth, is highlighted by manufacturers. Generally, they contain low concentration of HP (1.5%) and sodium hexametaphosphate to prevent the deposit of new stains. Their bleaching action is very limited and their use should be made with caution, since there is risk of irritation of the oral mucosa. [44]

Varnishes

These products are applied on the teeth surface (like nail polishes) and contain either HP or CP.

A few studies have been conducted searching the ability of varnishes to bleach teeth, without having very promising results [45,46]. Possible cause for this, is the short time that varnishes stay in contact with the enamel before getting dissolved.

Adhesive tapes

Tapes were proposed as an economic alternative to tooth whitening. They adhere to the anterior teeth and release for a short time (5-60 min) their active ingredient, which is HP at a low concentration (5-14%). Note that 10% concentration of CP is equal to a 3.3% HP. The results of their use are quite promising, but with significant side effects (mainly hypersensitivity) [47,48].

Effectiveness of OTC products

The clinical documentation of OTC bleaching products' effectiveness is not easily available since there is no common, reproducible and evidence-based color measurement method that is used. Thus general information derived from those articles cannot safely be mentioned [49, 50]. However, the most repetitive finding is that the adhesive tapes are more efficient than all other types of OTC products [51-53].

Toxicity of OTC products

The production of HP in the human body is followed by the release of free radicals via enzymatic reactions. These free radicals of endogenous HP production within the human cell, tend not to permeate the cell membrane, or to cover long distances within the cell, but to remain in it, maintaining a minimum balance due to the cell's survival effort. The problem of toxicity because of peroxides that may be included in the composition of the OTC products (HP, calcium peroxide [43]), which are usually combined with various natural chemical substances, such as mastic, aloe, papain, sodium citrate, sodium pyrophosphate, sodium tripolyphosphate, sodium hexametaphosphate [43], that have not been accused of toxicity, can only occur in people with akatalasia (absence of catalase enzyme that decomposes peroxides). In these individuals the function of leukocytes (migration and phagocytosis) results in the release of HP which, because of the absence of catalase, accumulates into the periodontal tissues causing necrosis and ulceration of the hard and soft tissues [54,55] or intense edema and necrosis.

Especially for HP-contained mouthwashes, it is stated that the contact of 3% HP mouthwash with already injured tissues, worsens the trauma and thus delays healing [56,57]. Generally, over- and long-term use can lead to intolerance, inflammation of the soft tissues, dryness, ageusia, hyperplasia of tasty papillae and wide whitening of the soft tissues of the oral cavity [56,57]. Finally, toothpastes with low HP content have a positive effect on limiting the microbial population in the mouth, without soft tissue lesions or irritations [58,59].

In conclusion, the OTC products are safe and non-toxic. However, it is necessary before administration and in order to avoid possible side effects, a thorough check of the patient's mouth to be made. In addition, their long-term application should be avoided. By fulfilling these prerequisites, as well as those recommended by the manufacturer, their use does not pose any risk and it could be beneficial, due to the local antisepsis that they prevail.

BLEACHING PROTOCOLS

The number of references on vital teeth bleaching is far from negligible. Searching on PubMed about the terms "dental" AND "bleaching" AND "protocols", leads to 56 results. If even the word "protocols" is skipped, the results are ejected to 2121 (data up to 12/2015). In order to study the available literature on different vital teeth bleaching protocols and make the relevant comparisons, mainly about their effectiveness, the previous number can be finally reduced to 39 articles. Comparative reference is made according to the results of a relevant to this subject diplomatic paper [60]. These studies were divided into in vivo and in vitro studies. Prior to the comparison and evaluation of the bleaching protocols described in this paper, it is appropriate to briefly refer to the color measurement methods and ways of tooth bleaching results' interpretation.

Color Measurement Methods

In most studies the following color measurement methods were applied: a) the color guide (Vita classic- Vita 3D Master), b) the colorimeter, c) the spectrophotometer, d) digital photos and photographic software and e) the QLF device (photo-induced fluorescence).

The use of the color guide was made in 5 in vitro studies (21.7%), of the colorimeter in 7 (30.4%), of the spectrophotometer in 10 (43.5%) and of QLF device in one study (4.3%). In clinical studies, the use of the color guide was made in 11 trials (50%), the colorimeter in 4 (18%), the spectrophotometer in 5 (23%) and the digital picture in 3 (14%). Total percentages corresponding to each identifying medium are: color guide (35%), colorimeter (24%), spectrophotometer (33%), digital photos and photographic software (7%), QLF device (photo-induced fluorescence) (2%). The conclusion from all studies is that identifying the teeth color is more accurate by using a device, especially a colorimeter and a spectrophotometer. This relates mainly to the fact that the devices are unaffected by the lighting conditions, the fatigue of the eyes, changes in environmental lighting conditions and repeatability of measurements [61]. The colorimeter, especially, according to the bibliography is the option with the lowest risk of errors and high accuracy and repeatability rates in measurements [17,62-70]. This result is enhanced by studies comparing different color measurement methods [15,50,62-66,71,72].

Evaluation of bleaching data

For the evaluation of results derived from bleaching procedures is necessary to analyze how the coordinates of the color (L*, a*, b*) behave when the shade of a tooth varies either to the darker (for example appearance of stain after sinking and staying in tea) or to the whiter (for example after treatment with bleaching products). The factor L* (Lightness) in the CIE Lab system expresses all information of the brightness of image, taking values from 0 (black) to 100 (white). The factors a* and b* express information about the color, with no numerical limits, although usually their values range from -120 to +120. Positive a* values represent shades of red, while negative values those of the green shades. Positive b* values represent shades of yellow, while negative b* values the shades of blue. The CIE Lab system is usually used for determining color differences, which can be calculated as values based on the equation [73]:

$$\Delta E^* = [(\Delta L^*)^2+(\Delta a^*)^2+(\Delta b^*)^2]^{1/2}.$$

The greater the difference of ΔE*, the easier for the average observer to detect the color change [74]. It should be noted though, that measuring only the difference ΔE* is not sufficient in order to have information spherically and completely about the actual final color of the object under study, that in case of bleaching techniques, is the buccal surface of the tooth. This is because this difference gives limited information about the real hue of the object. Indeed, as reported by Llambés et al. [38,75] equal changes of ΔE* can often create different visual perception of color change. So the ΔE*, as noted is not by itself a valid identifying parameter of color change among different teeth. The changes that are observed after bleaching and indicate bleaching effect is the upward movement of the L* and downward of a* and b*. Usually, the change in L* is greater, followed by b* and last by a*. Based on these data, it becomes obvious that the way that parameters L*, a*, b* and ΔE* is changing, should be interpreted. Generally, the greater the difference in ΔE* is, the greater the variation in color. But it has been supported, as mentioned above, that the calculation of ΔE* itself has no practical significance without the definition of two important limits which are the clinical perceptibility threshold (PT) and the acceptability threshold by the average observer (AT) [76*]

It is commonly accepted that the above mentioned thresholds, should be listed in ΔE* values. But there is no consensus among researchers on the values of ΔE* for these thresholds. Generally, it is argued that ΔE* value equal to 1 is visually discernible in 50% of the cases [76]. So ΔE* = 1 for the PT value tends to prevail. In other words, 50% of the observers will report that they start to distinguish difference between two samples when ΔE* gets at least the value of 1. Regarding the threshold AT, the data are slightly more complicated. In the bibliography there are

reports that support ΔE* values between 2 and 5.7 [78]. Only 1/3 of the relevant studies support a ΔE* value of 3.7. In other words, 50% of the observers reported that the difference between two samples is clinically acceptable when ΔE* has a value of 3.7 [76].

Two in vivo studies are particularly interesting because they attempt to quantify, in clinical conditions, the limits PT and AT. In the study of Douglas et al.[77] a complete denture was used, in which the upper left incisor had the ability to change. An edentulous patient wore this denture and participants evaluated its color. In the study by Da Silva et al.[78] two metal-ceramic crowns for one central upper incisor were constructed for 36 patients using either color guides or digital spectrophotometer for color measurement. Three calibrated evaluators compared the color of each crown to that of the adjacent natural central incisor. The results for PT in both these studies gave a value of ΔE* = 2.7. Based on this information and for easier comparison and evaluation of teeth whitening results, the threshold for PT should have the value of ΔE* = 2.7.

Conclusions about contemporary bleaching protocols

In vitro studies

From 20 in vitro studies, that were selected for this review based on the criteria RIS, 13 of them used human teeth (mostly anterior) while the rest 7 studies, teeth of bovine origin. The protocols that were tested were: a) 8 studies with bleaching technique only in office (one or more applications of HP-no trays or applications of 35% CP-with trays) , b) 5 studies with bleaching technique only at-home (applications of CP up to 22% with trays), c) 6 studies with bleaching techniques only in-office to techniques only at-home, and d) 1 study with bleaching techniques only in-office to only at-home and to combined protocol at-home/in-office.

In 9 of these studies, tooth staining was applied (with tea, wine, blood, etc.) prior to the application of the bleaching protocol. The main disadvantage was that the number of samples in vitro studies is considered insufficient for reliable data, with the exceptions of the study of

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** PT: Clinical perceptibility threshold: the color difference which is clinically distinct from/to 50% of the observers/measurements*

AT: Acceptability threshold of the average observer: the color difference which is considered acceptable by 50% of the observers.

Koniaris [60] in which each experimental group had 25 human teeth and Kielbassa et al. [50] study with 40 human teeth in each experimental group.

For the aforementioned information it is derived that only the study of Koniaris [60] examines the efficiency of the combined in-office and at-home bleaching protocol towards the single in-office or at-home protocol. In this study [60], the natural teeth were kept in a remineralization solution [79]

and the following bleaching protocols were applied: 1) Group 1 (BH): 15 at-home applications of 10% CP (Opalescence PF) for 2 hours/day. The applications were performed for 5 days with a 2-day interval, 2) Group 2 (BO1): 3 successive in-office applications of 40% HP (Opalescence Boost) for 15 min/per application and repetition of the procedure after a week, 3) Group 3 (BO2): 2 successive in-office applications of 40% HP (Opalescence Boost) for 15 min/per application and repetition of the procedure with one week interval between them and 4) Group 4 (BH+BO1): 15 applications of 10% CP (Opalescence PF) for 2 hours/day. Initially, this application was performed for 5 days with a 2-day interval. Then it was followed by 3 consecutive 40% HP in-office applications (Opalescence Boost) for 15 min/per application with one week interval. Considering the threshold of PT value at 2.7, the results revealed that there was no statistical difference in the bleaching effect among the previous described bleaching protocols for any examining period, up to six months. Differences among the individual color parameters were though detected. Moreover, it is interesting to mention that the most significant relapse at six months was detected for the at-home bleaching group (lower brightness-L* and highest ΔE*). On the other hand, the combined protocol group (at-home and in-office), retained the whitening effect six months after the completion of the treatment (higher brightness-L* and lowest ΔE*), while it showed the best bleaching effect immediately after completion of the bleaching process. Generally, studies that correspond to these findings (except of the results of the combined protocol), seem to be the majority, such as the studies of Wiegand et al.[80] and Auschill et al.[81]. Regarding the at-home bleaching protocols, there are two in vitro studies suggesting no statistically different results regardless the used concentration of CP. More specifically, Borges et al.[82] (bovine teeth) and Sulieman et al.[63] (human third molars) compare concentrations of 10 to 16% CP and 10 to 15%, 20%, 22%, 30% CP respectively. In each group a bleaching effect was achieved with no statistically significant difference between them. Generally all in vitro studies verify an equal result for both at-home and in-office bleaching protocols.

Clinical studies

From the relevant clinical studies, 21 were selected to be reported in this paper, all of which involved anterior teeth. The protocols that were tested were: 1) 4 studies with in-office bleaching technique only (one or more HP applications without trays), 2) 10 studies with at-home bleaching technique (applications with trays), 3) 3 studies with combined bleaching technique (applications with trays), 4) 2 studies with only at-home vs only in-office, 5) 2 studies with only at-home vs combined technique.

In regard to the clinical studies, only three [32,37,82] compare the efficiency of the combined bleaching protocol with the other ones. In the first study of Kugel et al.[32], the efficacy of the combined protocol is compared to the in-office one. Despite the low number of participants (20 adults) and the short duration after the end of the procedure (only 5 days), the authors claim that they found a significant superiority of the combined protocol (35% CP x 2x15min and 15% CP at-home for 5 days). Regarding the second study [37], the comparison of the combined protocol versus at-home was made with a color guide and a spectrophotometer for a period up to four months after bleaching. The results were promising for the combined protocol, showing a slight, non important superiority, only for the first two weeks. Noteworthy is the abscess of relapse phenomenon which is in contrast to the majority of other relevant studies. The third study of Dawson et al.[82] had 3 groups of 12 people and identified the change of color in the six upper anterior teeth using a color guide. There was a statistically significant difference for the at-home and in-office groups but not clinically noticeable. In general the efficiency of the combined protocol versus at-home or in-office ones is not statistically different while sometimes data is contradictory.

From the clinical studies one could mention those of Meireles et al.[85] and Grobler et al.[80]. The first was a double-blind study on 92 volunteers which measured color changes of the six maxillary anterior teeth, with a color-guide (Vita Classic) and a spectrophotometer (Vita Easy Shade). The application of 10% and 16% CP (2h/day for three weeks) gave statistically identical values of ΔE*, one week ($\Delta E^{*10\%}$=4.3±1.9 and $\Delta E^{*16\%}$=4.6±2) and 6 months after ($\Delta E^{*10\%}$=3.9±1.4 and $\Delta E^{*16\%}$=4.5±1.7). Finally, in the survey of Grobler et al.[80], 34 patients were divided into two groups and were treated with at-home bleaching (trays with 10% CP), but using two different products (Opalescence PF vs Nite-White). As expected, the two products achieved similar result immediately after (ΔE* = 5.2) and 6 months later (ΔE* = 4.2).

Additionally, in the split mouth study of Bernardon et al.[82] at-home, in-office and combined bleaching protocols were tested with a spectrophotometer and a color guide. Although numerically superior, the combined protocol had no significant difference four months later (ΔE^{*home}=9.7, $\Delta E^{*office}$=8.98, $DE^{*combined}$=10.32). This finding is reported also elsewhere [60]. Finally, in the review of Cunha et al.[39], the authors concluded that the combined and in-office protocols seem to have slightly better results one week after treatment, but thereafter no difference was detected. It is worthy to highlight the fact that in this review only 5 articles (out of 483 initially) were finally used, since strict selection criteria were set and as stated above, the monitoring time in most studies did not exceed 2-4 weeks after bleaching. The combined

bleaching protocol (in-office and at-home), is only applied in four studies [1,32,39,82]. Its direct comparison to different protocols, either at-home or in-office is done just in two studies [32, 82.] More specifically, the benefits of the combined protocol are supported in the clinical studies of Deliperi et al.[1] and Bernardon et al.[82] In general it seems that most in vitro and in vivo studies agree that there is not a significant difference but only a small numerical trend in favor of the combined protocol.

Duration of bleaching monitoring and relapse process

Regarding the testing period of bleaching studies, only two of them conducted color measurement up to six months. The first is the study of Meireles et al.[71] and its outcome reported no statistically significant difference between the two at-home groups (10% and 16% CP), six months after bleaching. They mentioned, also, that the consumption of foods which contain many pigments had no effect during this period. The second study is that of Grobler et al.[61] These authors compared two different 10% CP at-home products. The products achieved a similar result just after bleaching ($\Delta E^*1=5.29$ vs $\Delta E^*2=5.2$) and a significant different after 6 months ($\Delta E^*1=4.25$ vs $\Delta E^*2=3.87$).

The phenomenon of "color relapse" is present in the majority of studies. Usually, it takes place since the first week after bleaching and in most of the cases, tends to stabilize after 4-6 weeks.

Therefore, based on current data, the combined bleaching protocol seems to outweigh the at-home and/or the in-office ones. However, this superiority is not statistically significant, whereas it refers only on the ability of a smaller relapse within six months and not on the ability of achieving a better bleaching effect, which seems to be almost the same in all three protocols.

RECOMMENDED AT HOME BLEACHING PROTOCOL

There are certain steps to be followed on selecting a case for bleaching:

✓ *Evaluation-selection of the case:* The indications for applying a bleaching technique generally include adults with teeth at shades mainly A and/or B, with no intense endogenous discolorations, without prosthetic restorations and extended white spots or other areas with extensive decalcifications and erosions. Also, poor-performed prosthetic and/or conservative restorations with microleakage, primary and/or secondary and root caries, periodontal inflammation, generalized and/or localized periodontitis/gingivitis and bruxism are contraindications. Reasons for hypersensitivity should be checked and preventive measures should then be applied. Any condition that could cause pain, microleakage or inflammation should be eliminated before the application of a bleaching agent. Not a safe indication for bleaching is finally pregnancy. Smoking is no longer considered as a contraindication, but it is

recommended to be reduced, at least during the use of bleaching products.

✓ *Initial color selection.* Color identification takes place under natural daylight with shades from the Vitapan Classic and the 3D Master color guide (Vita, Bad Sackingen, Germany), arranged in a brightness order (Figure 2). At the same session, the dentist holding the selected color guide next to the natural teeth (mainly upper incisors) is taking photographs of the arches and the smile for extra documentation.

According to Vitapan classic color guide (with the shade B1 as the most bleached)

B1	***A1***	***B2***	***D1***	***A2***	***D2***	***C2***	***D3***	***A3***	***D4***	***B3***	***A3.5***	***B4***	***C3***	***A4***	***C4***

According to the 3D Master color guide (with the shade 0M1 as the most bleached)

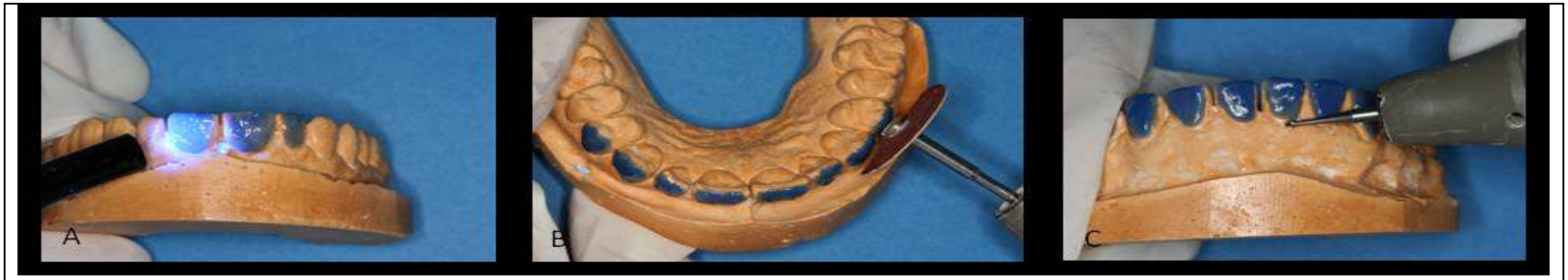
0M1	***0.5M1***	***1M1***	***1M1.5***	***1M2***	***1.5M2***	***2M2***	***2.5M2***	***3M2***	***3.5M2***	***4M2***	***4.5M2***	***5M2***	***5M2.5***	***5M3***

Figure 2: **Modified series of color indices of the color charts Vitapan Classic and 3D Master (Vita, Bad Sackingen, Germany).**

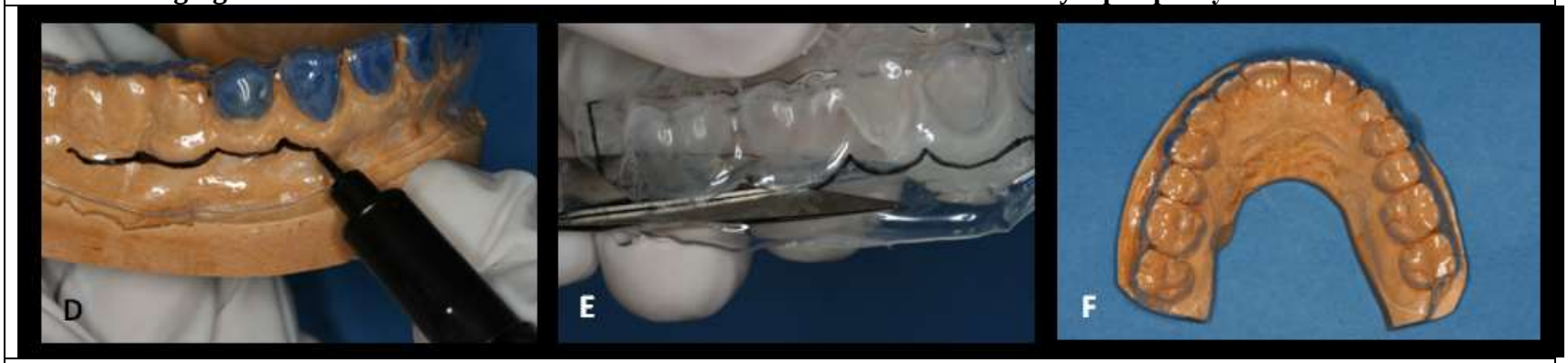
✓ *Examination and preparation of the oral cavity*. The examination of the oral cavity, before the application of bleaching products, includes checking the existing restorations for microgaps and reasons for microleakage, cracks or fractures. In such cases old restorations may be replaced temporarily with glass ionomer cements and microgaps repaired with flowable resins. Treatment of gingivitis/periodontitis and of any other endodontic and/or periodontic problem should be arranged before bleaching.

✓ *Taking impressions and construction of custom-made trays.* Impressions are taken with an alginate material and commercial trays. Information on the construction of the custom-made trays is given in Table 2.

Table 2: Instructions for construction and use of bleaching custom-made trays



A. Creating space for the bleaching material by placing the special resin included in the package or any old flowable resin. B. Polishing the surfaces in order to have the same thickness everywhere (0,5mm). C. Creating a groove on the limits of the gingival sulcus in order to create obstruction for the material in the tray's periphery.



D. The tray's periphery is placed 0,5-1,00 mm beyond the gingival sulcus, at the mucosa. E. The tray is cut with scissors following the gum line. F. The tray is checked on the cast.

✓ *Effective presentation and explanation of the instructions for use and application of the chosen product.* The trays are checked in the mouth in order to cover the palatal region of the teeth up to 1,5mm from the gingival margin without causing any discomfort or pain. The way of applying the material in the trays is shown right at the individual tray of the patient. The patient wears the trays and leaves the office with the trays in his mouth. All instructions should be given to the patient in an oral and written way (Table 3).

Table 3: Instructions of use for at-home bleaching products.

BLEACHING AT-HOME. INSTRUCTIONS FOR THE USE OF BLEACHING MATERIAL AND TRAYS
To achieve the desired bleaching results the following instructions should be applied **thoroughly** :
1. The bleaching product which is suggested for your teeth, is designed **exclusively for dental use** and is recommended by your dentist.
2. The tubes with the material should be stored in a **cool and safe** place in the refrigerator (keep away from the reach of children). **CAUTION at the expiration date!**
3. Keep the trays with the material in your mouth, only **for x hours** per day *(suggest time of application according to manufacturer's directions of use).*The placement of a large amount of material in the trays does not accelerate the process of bleaching. **Save the material in order to prevent symptoms, but also to use it for more days.** The first two days apply the trays with the material for x hours per time, 2 times per day. The next day follow the given program of application. Do not sleep with the trays on except if otherwise suggested. During the procedure the material can be mixed with your saliva so split carefully without rinsing until you remove the trays from your mouth completely.
4. Brush thoroughly your teeth before and after the application of the bleaching agent and use dental floss. After the use of the material, you should keep good oral hygiene. You can also use a whitening toothpaste for the enhancement of the bleaching effect during the period of the treatment. **Always rinse your mouth well.**
5. During treatment, please use a fluoride mouthwash of your choice, at least once a day.
6. Avoid eating or drinking immediately after removing trays for at least 1-2 hours. Avoid alcoholic or carbonated beverages (red wine, coffee, tea, refreshments such as Cola etc.) and acidic foods .
7. If you feel sensitivity in your teeth, stop using the material for a day. If the sensitivity continues you should inform your dentist.
8. Smoking should be diminished during the entire procedure. Avoid smoking for at least 1-2 hours after the removal of the trays.
9. Keep your trays always clean.
10. Finally, follow the schedule that is recommended by your dentist.

✓ *Recall appointments.* The patient should be seen once a week in order to ensure proper compliance to the instructions and to maintain his interest on the process until its completion. Documentation of color changes with photographs should be taken in every recall appointment.

✓ *Completion of the procedure and outcome's assessment.* All data collected during the recall appointments should be kept on the patient's file. Description of the technique and materials used as well as results and possible side effects for future review should be also reported (Table 4).

Table 4: Bleaching procedure form

BLEACHING PROCEDURE FORM	
Patient's name/surname:	
Address: Telephone number:	
Age:	
Cause for bleaching:	
Suggested by: Dentist: Patient: Other:	
History of tooth bleaching: first time: YES NO	
Previous experience on bleaching:	
AT-HOME BLEACHING	
Initial shade identification:	Vita Classic: 3D Master:
Product	Duration
Shade identification at 7 days	Vita Classic: 3D Master:
Product	Duration
Shade identification at 14 days	Vita Classic: 3D Master:
Product	Duration
Discontinuation of the treatment	YES NO
The discontinuation took place because of: 1) Hypersensitivity….2) Lack of time…. 3) Difficulties in use….4) Unpleasant flavor….5) Burn….6) Other……	
Recall at 30 days	
Shade identification	Vita Classic 3D Master
Other findings/instructions	
Recall at 6 months	
Shade identification	Vita Classic 3D Master
Other findings/instructions	
Recall at 12 months	
Shade identification	Vita Classic 3D Master
Other findings/instructions	
IN-OFFICE BLEACHING	
Initial shade identification	Vita Classic: 3D Master:
Product	Duration
Shade identification 1st session	Vita Classic: 3D Master:
Product	Duration
Shade identification 2nd session	Vita Classic: 3D Master:
Product	Duration
Bleaching device	YES NO

Type of the device	
Discontinuation of the treatment	YES NO
The discontinuation took place because of: 1) Hypersensitivity….2) Lack of time…. 3) Difficulties in use….4) Unpleasant flavor….5) Burn….6) Other……	
Recall at 30 days	
Shade identification	Vita Classic 3D Master
Other findings/ instructions	
Recall at 6 months	
Shade identification	Vita Classic 3D Master
Other findings/ instructions	
Recall at 12 months	
Shade identification	Vita Classic 3D Master
Other findings/ instructions	
COMBINED BLEACHING TECHNIQUE	
A) AT-HOME BLEACHING	
Initial shade identification	Vita Classic: 3D Master:
Product	Duration
Shade identification at 7 days	Vita Classic: 3D Master:
Product	Duration
Shade identification at 15 days	Vita Classic: 3D Master:
Product	Duration
B) IN-OFFICE BLEACHING	
Initial shade identification	Vita Classic: 3D Master:
Product	Duration
Shade identification 1st session	Vita Classic: 3D Master:
Product	Duration
Shade identification 2nd session	Vita Classic: 3D Master:
Product	Duration
Bleaching device	YES NO
Type of device	
Recall at 30 days	
Shade identification	Vita Classic 3D Master
Other findings/ instructions	
Recall at 6 months	
Shade identification	Vita Classic 3D Master
Other findings/ instructions	
Recall at 12 months	
Shade identification	Vita Classic 3D Master
Other findings/ instructions	
Discontinuation of the treatment	YES NO
The discontinuation took place because of: 1) Hypersensitivity….2) Lack of time…. 3)Difficulties in use….4) Unpleasant flavor….5) Burn….6) Other……	
The discontinuation took place: In-Office:…. At-Home:….	

✓ *Guidelines for the maintenance of the bleaching effect.* The guidelines should be written in a leaflet with all instructions for the procedure. Special caution should be taken for the

reduction of food with pigments (e.g. mustard, beetroots, turmeric etc.) or drinks such as red wine, sparkling beverages like Cola etc.

✓ *Comments about the cost of the process*. Technical stages and materials to be used should be clarified. The cost of the procedure should be then relevant to the cost of the material and relevant expenses. The patient should understand whether the cost of the procedure includes the price of the material for both arches and for the period of the treatment (Table 5).

Table 5: Bleaching consent form

COST OF BLEACHING TECHNIQUES	
Depending on your initial tooth color, the degree of whitening you want to achieve, the time you are willing to devote and the cost you can afford the following options can be considered:	
1. Basic technique (first degree) (14 days at-home): At-home application of the bleaching material with custom-made trays for 14 days (application 2-3 hours/day):..... €/$.	
2. Combined technique (at-home & in-office) (second degree) (14 days at-home and 2 sessions in-office): 1) at-home application of the bleaching material with custom-made trays for one week (application 2-3 hours/day), 2) one session (2x15min) in-office (no bleaching device), 3) at-home application for another 5-6 days, 4) second session (2x15min) in-office (no bleaching device): ..... EURO. Every additional session in-office is charged ..... €/$.	
3. Rapid bleaching (in-office) (third degree) (3-4 sessions in-office): It takes place only in-office (2x15min per session): ..... €/$/per session.	
The cost of all categories includes the cost of the material unless otherwise stated.	
-The final whitening effect cannot be predetermined. Additional process and charge will be discussed with you at the end of the basic technique. -Bleaching as described in this form is absolutely safe for teeth and overall health. Please follow instructions carefully. Do not hesitate to inform us on any discomfort or problem you may face during treatment. The dentist has no responsibility whatsoever on symptoms occurring through irrational use of the material and for storage conditions which are different from those described in the " Instructions for the use of bleaching materials and trays" form. -By signing this form you agree that you are fully informed about the procedure and its cost and you agree fully to its implementation.	
Your dentist	The patient
	I am aware

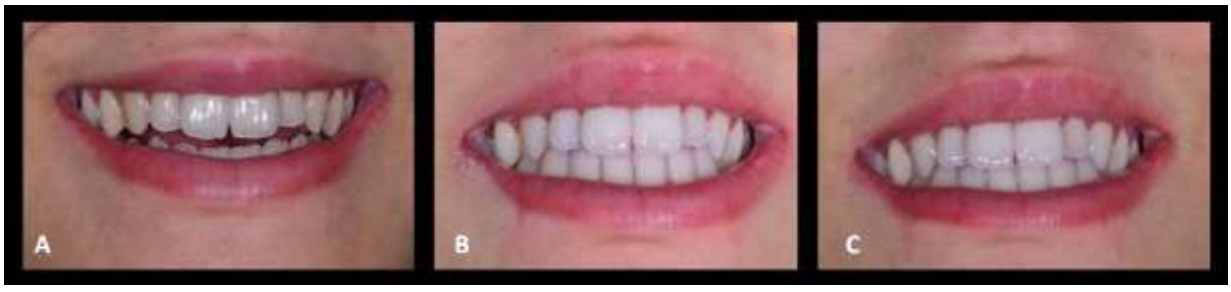
Instructions for choosing the concentration and composition/technique of the bleaching material according to the degree of transparency/opacity of the teeth, type of discoloration and age of the patient, are shown in Table 6.

Table 6: Guidelines for bleaching materials' selection and application time

Cases classification	
	*Natural dentition, teeth with a small relative transparency, A or B shades in individuals of 20-30 years old. (at-home/14 days)*
 	*Individuals of 30-40 years old with natural dentition (at-home/14 days or/and in-office/1-2 sessions-2x15min per session)*
 	*Individuals of 40 years old and above with natural dentition (combined at-home/30 days and in-office/2-3 sessions-2x15min per session)*
 	*Opaque teeth, with endogenous discoloration (e.g. 1st, 2nd degree of tetracycline staining). More intense discolorations (3rd degree of tetracycline staining and C,D shades) do not have very good results and demand a longer treatment (combined at-home/45 days and in-office/3-4 sessions-2x15min per session).*

For most patients, with shades of natural teeth A3, B3 (and/or brighter), at-home bleaching with 10% CP for 14 days is sufficient to achieve a shade around B1 or OM1/GM2/GM3 (Figure 3,4).

Figure 3:**Bleaching at-home: Woman, aged 20. Initial shade A2. Application of 10% CP for 14 days. Final shade B1 at 30 days.**



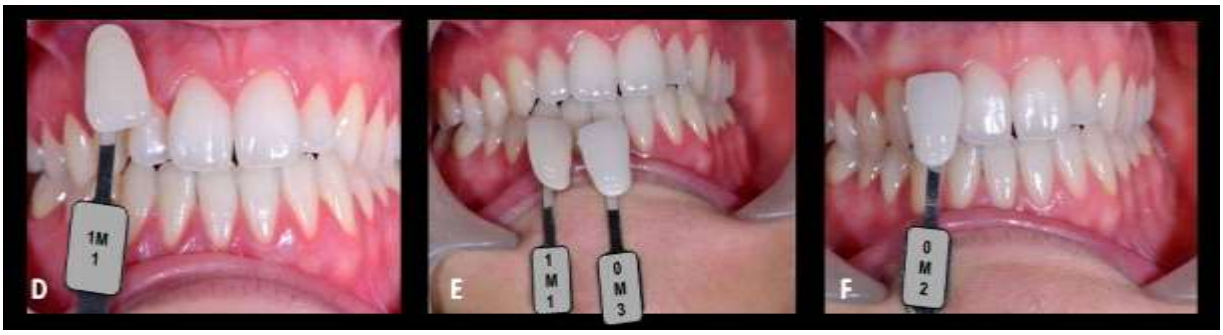


Figure 4:**Bleaching at-home: Woman, aged 25. A,B,C: Smile in 0,15,30 days respectively. D: Initial shade 1M1, E: Shade OM3 at 15 days with 10% CP, F: Final shade 0M2 at 30 days.**

On the other hand, teeth with darker shades, smokers or generally people over 40 years of age, require at least 30 days of 10 and/or 16% CP use (Figure 5,6). In-office sessions can be also suggested in these cases (See "Recommended in-office bleaching protocol" and "Recommended combined bleaching protocol" sessions for relevant cases).

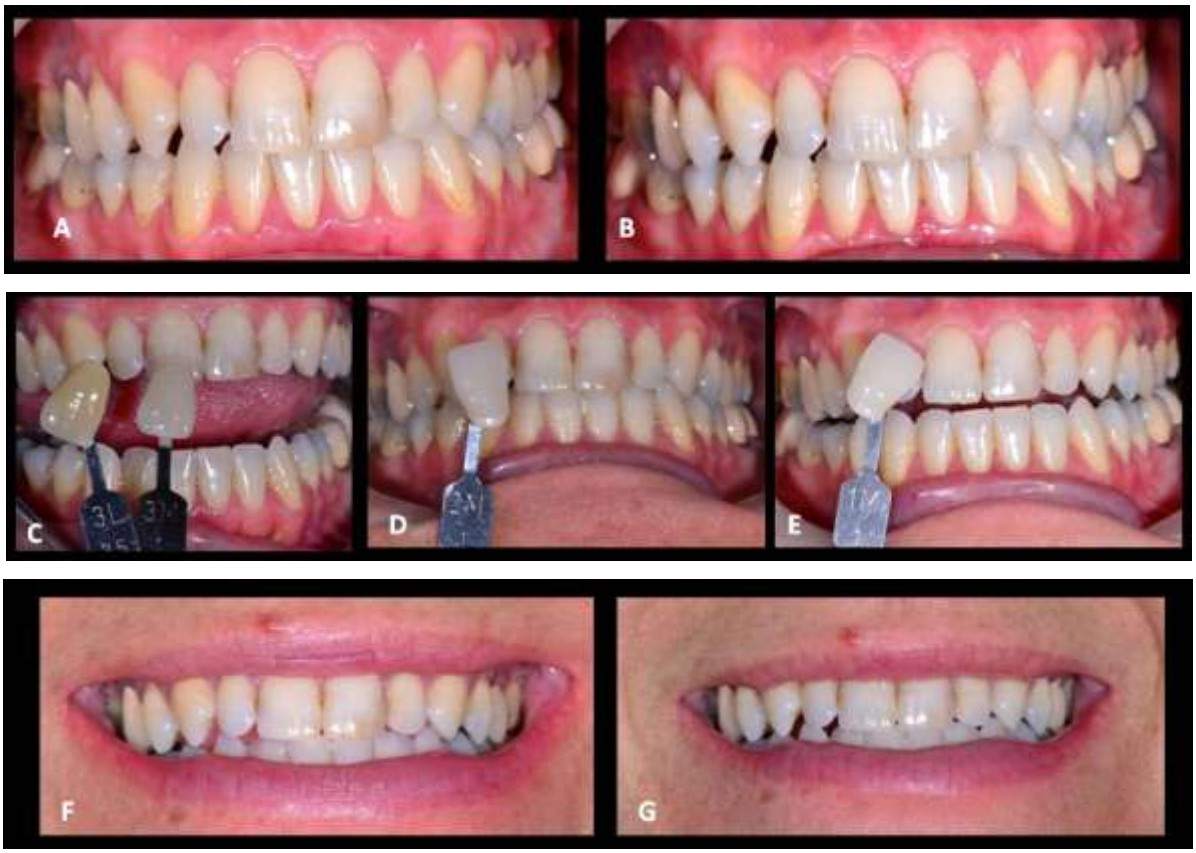


Figure 5. **Bleaching at-home: Woman, aged 45. A. Before bleaching, B. After bleaching at 45 days, C. Initial shade 3L2.5/cervical, 3M1/incisal, D. Shade 2M1 at 15 days with 10% CP, E. Final shade 1M1 at 30 days with 16% CP and at 40 days with 10% CP, F. Initial smile, G. Final smile at 6 months.**

Figure 6. **Bleaching at-home: Male, aged 47. A. Before bleaching, B. Initial shade A3.5, C. After bleaching with 10% CP for 30 days. Final shade 2M1.**

RECOMMENDED IN-OFFICE BLEACHING PROTOCOL

The in-office technique follows initially the steps 1-3, as they are mentioned in the section "Recommended Protocols: At-home Bleaching." The patient is then informed that in the next appointment bleaching material will be applied for 2x15min. He/she should be advised to carry a music player, book etc. for the waiting time in order to feel comfortable and relaxed.

Isolation of the soft tissues is of outmost importance during procedures in-office. The most effective and simple way of isolation is with the special block-out resin of various shades depending on the manufacturer, which is available in almost every relevant package. It is important to hold the tip of the syringe continuously within the mass of the still unpolymerized material, while applying the block-out resin over the gumline, in order to prohibit the creation of air bubbles. Optimally, the block-out resin can be placed in a thin layer within the gingival sulcus and polymerized and then in a thicker layer over the gumline where is finally polymerized. The block-out resin should be always checked for its hardness and integrity (Figure 7).

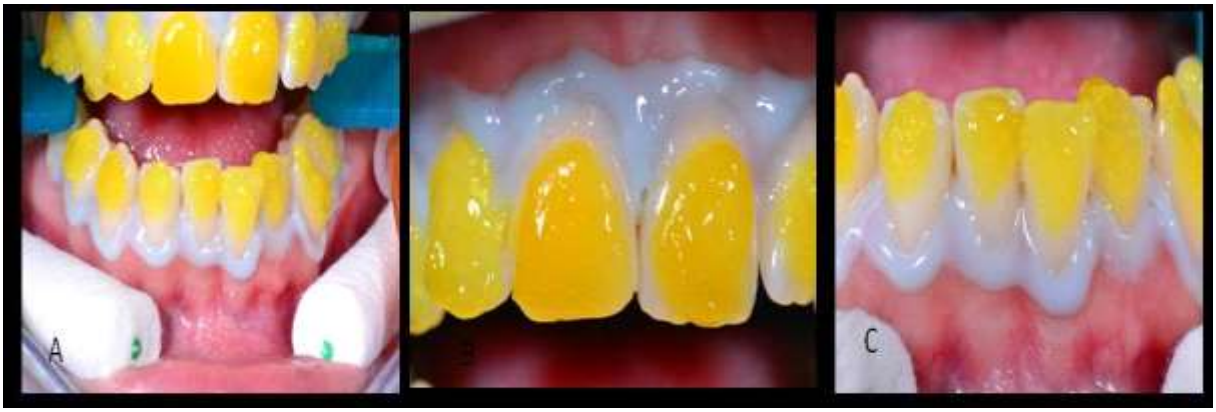


Figure 7: **Gums' isolation with block-out resin. The bleaching material is placed uniformly in thickness following the gum line.**

The contemporary bleaching products used in-office, are in packaging of self-mixed syringe with

intraoral tip, which makes easy the material's application on the labial tooth surface. After the application, the bleaching agent remains undisturbed for 15 min. The dentist should only periodically stir it with a disposable tip. During this period patients can note whatever they want to communicate with the dentist on a notebook. The removal of the material is done with extreme care and only with cotton dental rolls (without washing). Then the bleaching material is re-applicated for another 15 min and the previous procedure is repeated. In one session, the application of bleaching product is feasible for up to3 periods of 15 min each. Usually, 2x15min is the period that most patients afford to fulfill. The final removal of material is again performed with cotton rolls and then teeth and mucosa are well rinsed with the air-water syringe. After the removal of all means of isolation, the patient finally rinses his/hers mouth. Any micro-burns at the gumline are healed within 24 hours. Larger burns can occur at sites where the saliva ejector is resting because of local suction of the bleaching material. The in-office application can be repeated 1-2 times per week (Figure 8).

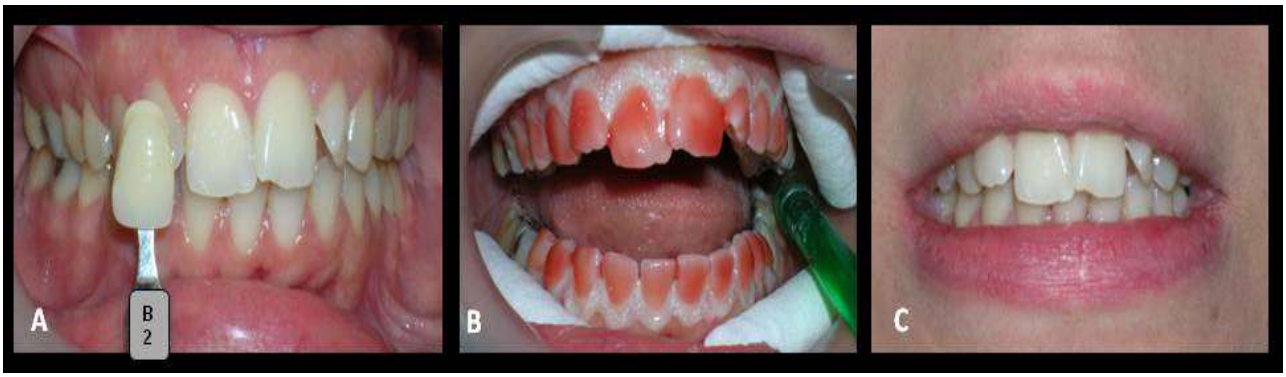


Figure 8: **Bleaching in-office: Woman, aged 32. A. Initial shade B2, B. One application of 35% CP (2x15 min), C. Final shade B1.**

Apart from the natural teeth color, age is another key factor determining the concentrations of the bleaching materials, as mentioned before. People up to 30-35 years of age should avoid undertaking in-office bleaching sessions but when done, 1-2 sessions should be enough. Conversely, in people over 35 years of age, the application of higher concentrations for 3-5 repetitive sessions in-office, are required in order to achieve an equivalent color change (Figure 9,10).

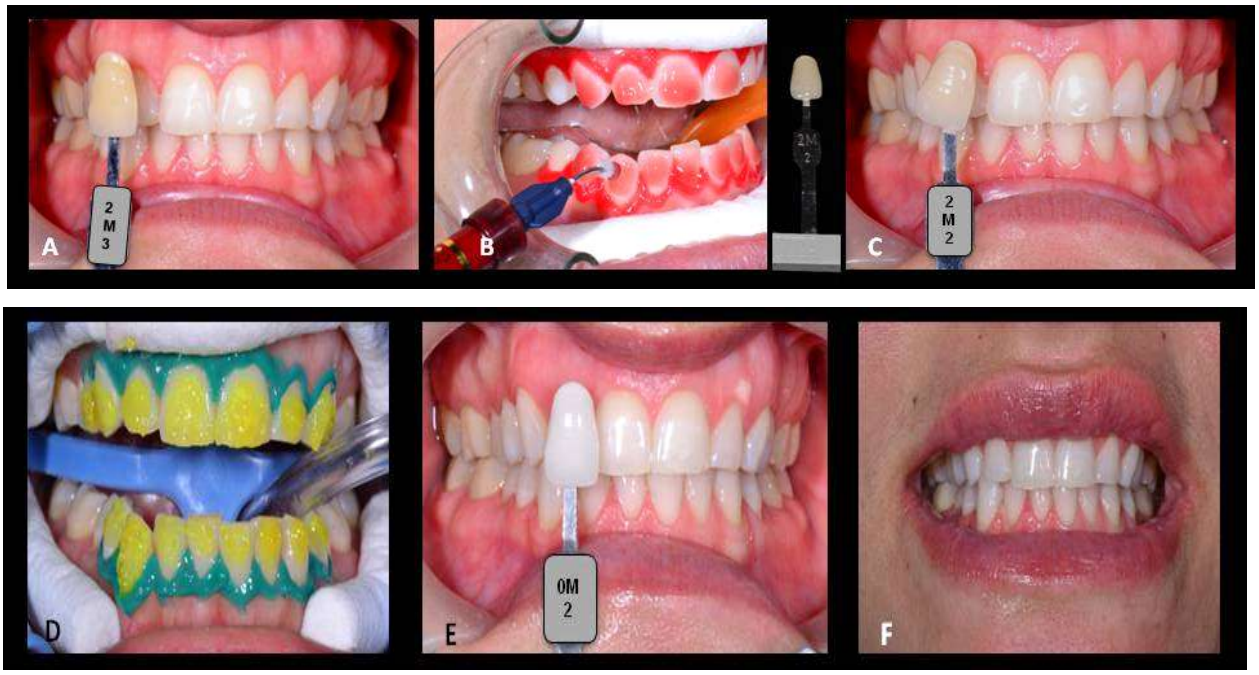


Figure 9: **Bleaching in-office: Woman, aged 37. A. Initial shade 2M3. B. One application of 40% CP (2x15min), C. Shade 2M2 after the first session. D. Four repetitive sessions with 35% CP (2x15min per session), E. Final shade OM2, F. Final smile at 45 days.**

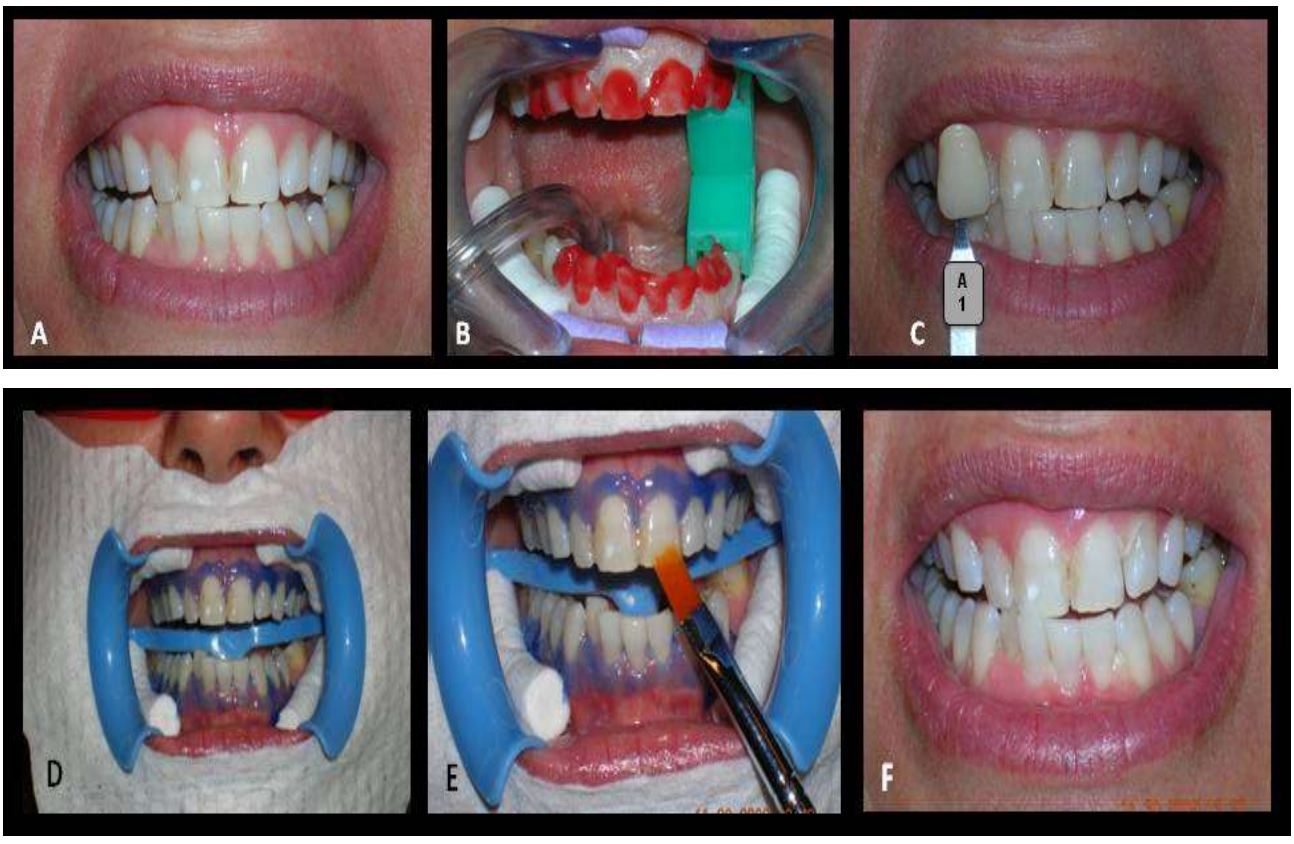


Figure 10. **Bleaching in-office: Woman, aged 45. A. Initial shade A2, B. One application of 35% CP (2x15min), C. Shade A1 after the first application, D. Isolation for the 2nd**

application, E. Third application of 35% CP (2x15min), F. Final shade 0M1 at 30 days.

RECOMMENDED COMBINED BLEACHING PROTOCOL

The combined protocol is considered as the most effective technique both in short and long term. Usually, 10% CP is applied in custom-made trays for five consequent days. Then, there is a break of two days, followed by the in-office session (2-3x15min with 35% HP). The following week the procedure is carried out at-home with either 10 or 16% CP. If needed a third circle could be followed. Usually, the process is completed when there are no further color changes. However, in cases of more intense discolorations or dark tooth shade (opaque A4, B4, D4, C4), the process may be continued for a fourth circle. Especially in zone-type discolorations, (1st degree of tetracyclines staining), the whole process can be carried out at-home with 10% CP for 2-3 months (Figure 11-13).

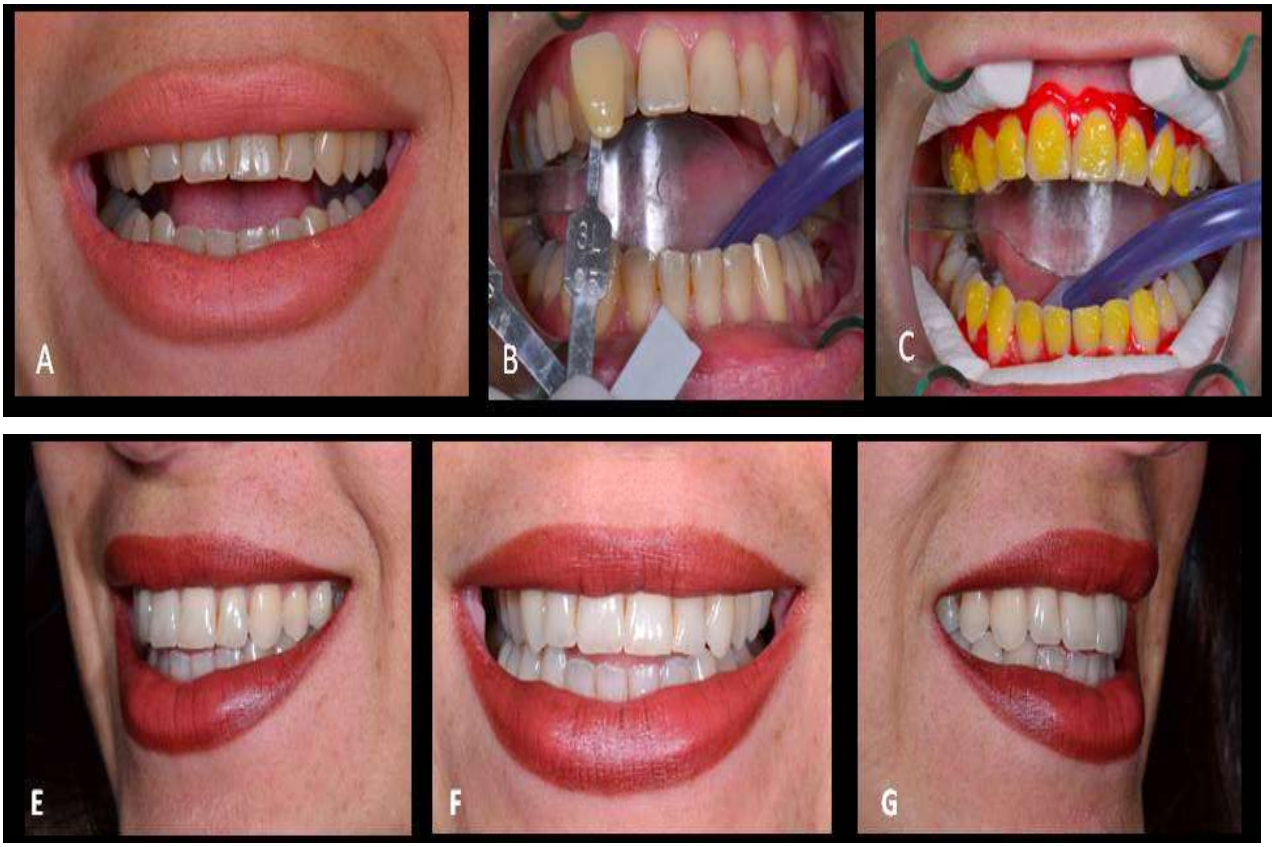


Figure 11: **Bleaching at-home and in-office (combined technique): Woman aged 35. A. Initial smile, B. Initial shade 3L1.5, C. In-office application of 35% HP (2x15 min), D-F. Final smile after another 30 days of application of 16% CP at-home.**

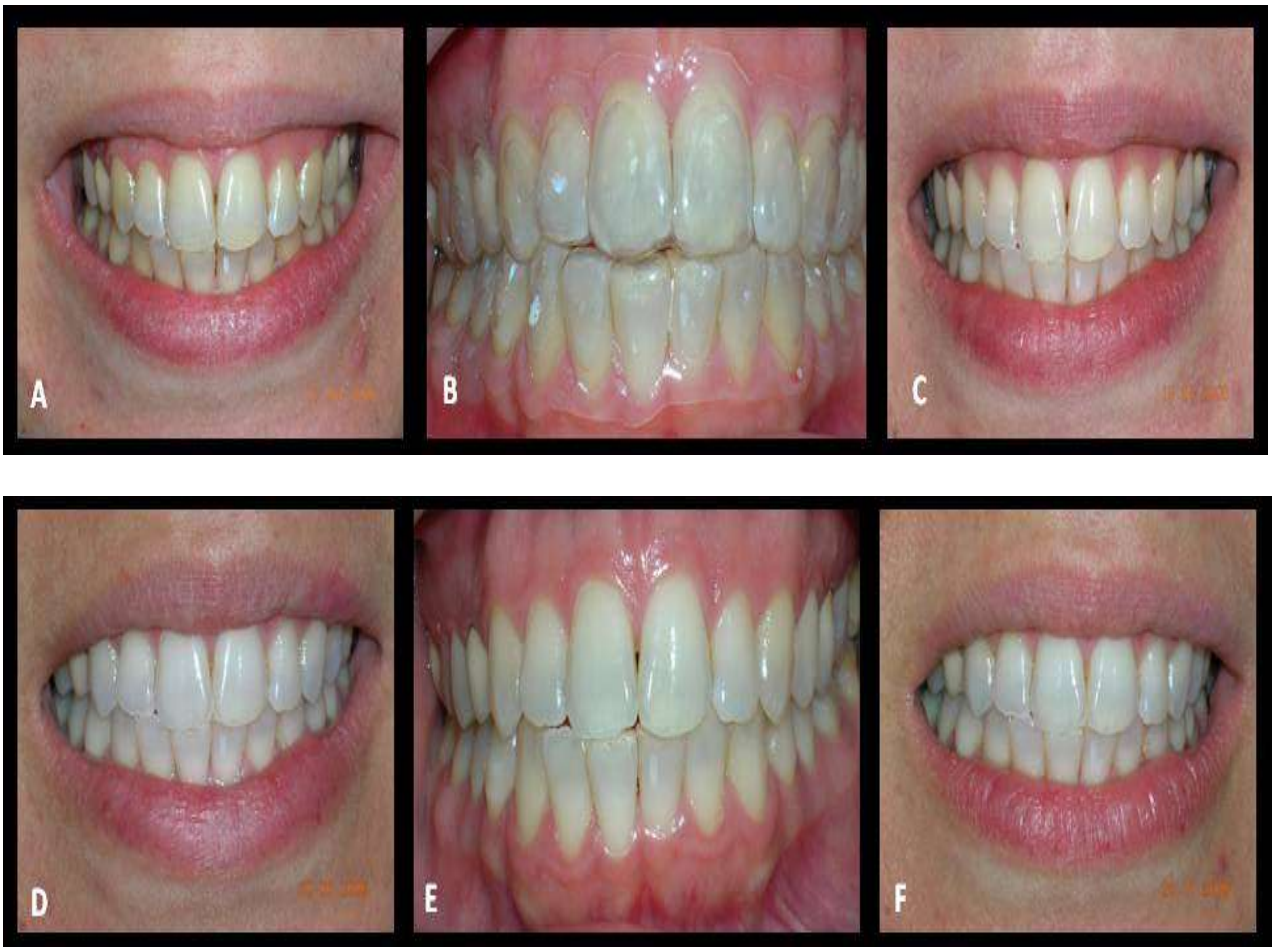


Figure 12: **C Bleaching at-home and in-office (combined technique): Woman, aged 30 with 1st degree staining from tetracycline. A. Initial smile (shade B3, main body of upper central incisors). B. Checking the customized guard in the mouth. C. After 15 days of 10% CP (shade B2), D. After 30 days of 16% CP and 2 sessions in-office with 35% HP (shade B2, B1), E. After the last 15 days of 10% CP (shade B1), F. Final smile after six months (final shade B1).**

For more intense discolorations (2nd, 3rd degree of tetracycline staining) and darker than A3 shades at over 40 years old patients or in other exceptional circumstances of intrinsic discolorations, the combined bleaching technique should be suggested (Figure 13).

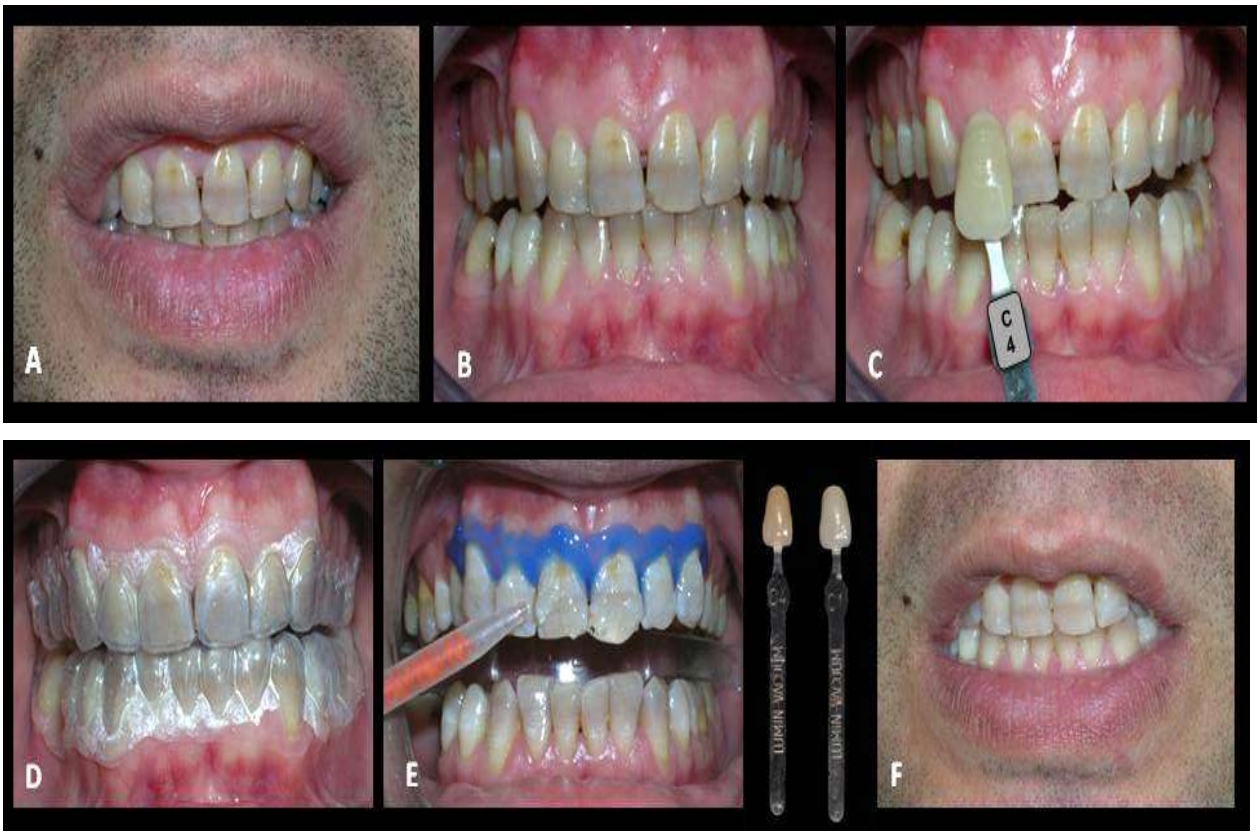


Figure 13: Bleaching at-home and in-office (combined technique). Male aged 37 with 2nd degree discoloration from tetracyclines. A,B. Initial smile, C. Initial shades C4 main body/ A3,5 cervical region, D. Application at-home of 10% CP for 10 days, following 16% CP for 45 days, following 10% CP for another 30 days, E. Application of 35% HP in-office, (2x15min) for four sessions, F. Final shade C1/A1.

SIDE-EFFECTS

The most common side effect of all bleaching procedures is tooth hypersensitivity and temporal discomfort because of inflammation or local burns of the gingiva. The last symptoms disappear within the next 24 hours. No medication is usually needed. In case of severe burns glycerin gel can be put extraorally and aloe vera mouthwashes can be used intraorally. Hypersensitivity, however, may remain longer and causes discomfort, thus there is a need for prevention. Intensive sealing of the pre-existing cracks could minimize such events since there is a positive although weak, correlation between the existence of cracks in the enamel and hypersensitivity [91]. Additionally, low concentration and especially the 10% CP is supposed to have a reversible hypersensitivity influence, depending on the type of tissue exposed to bleaching [92]. The cause of such an effect is the creation of oxygen bubbles into the dentinal tubules during the application of HP and the subsequent stimulation of the pulp. OTC products can also cause hypersensitivity

and gingival pain/irritation [94-99]. These symptoms can occur through false way or extended time of application [95,98], insufficient precaution measures, inadequate gingiva isolation [100], and pre-existing dentinal hypersensitivity, abrasions/erosions or gingivitis [99,101], as well as cervical caries and multiple restorations [102]. Because of its frequent occurrence during bleaching treatments, the concurrent application of desensitizing agents containing components such as potassium nitrate, sodium fluoride, calcium phosphate, fluoride varnish and adhesive agents is recommended, preventively, either at-home by the patient or in-office. Also another technical method proposed for reduction or elimination of the symptom, is the use of laser as an indirect analgesic assistance through repolarization of corrupt nerve membranes. Meanwhile the immediate pausing of the procedure and the simultaneous reduction of the concentration, duration and frequency of use of the bleaching material for the rest of the procedure is suggested. Furthermore topical agents such as fluoride gels or potassium nitrate are recommended. Studies have shown that tooth sensitivity returns to normal within a week [103]. Especially effective in the treatment of mild hypersensitivity is the application of materials with: 1) a complex of casein phosphopeptide (CCP) and amorphous calcium phosphate (ACP), known as Recaldent™ (CCP-ACP), found in patented products such as Paste MI and MI Paste Plus (GC Europe) and 2) calcium sodium phosphosilicate (NovaMin) found in Oravive (Glaxo Smith Kline).

Rarest to be found in the relevant literature is a possible external absorption case due to technical errors of the construction of customized guards [104] or an acute allergic reaction to peroxide with noisy clinical presentation (Figure 16). In case of such an allergic reaction, the use of the product should be promptly discontinued and the patient should seek for medical advice as soon as possible. In any case, perioral tissues usually return to normal within the next 10-15 days (Figure 17).

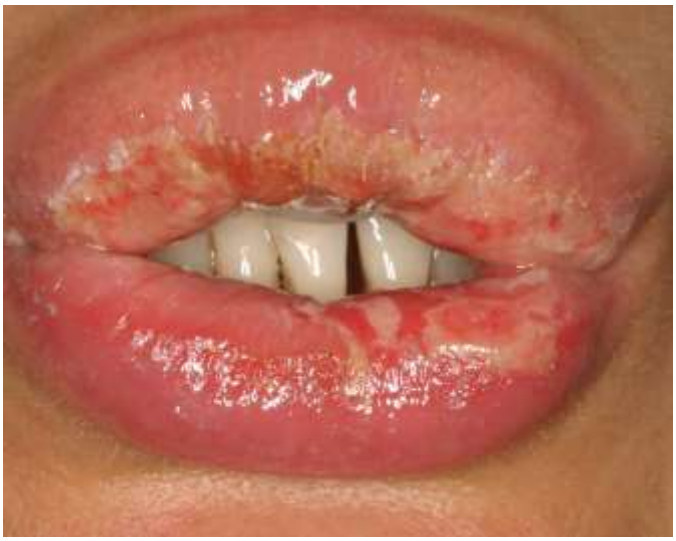


Figure 16: Allergic reaction to the bleaching agent with an intense extraoral clinical image. The immediate discontinuation of the process is recommended.

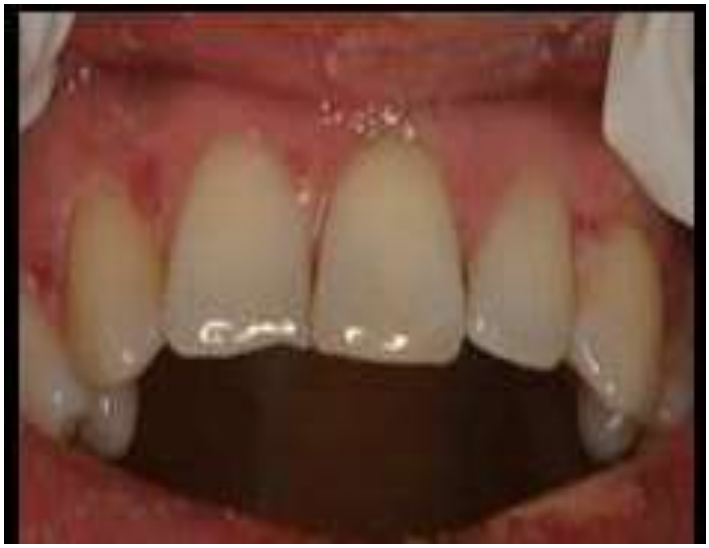


Figure 17: **The case in Figure 16, 15 days after the initial allergic reaction**

MAINTENANCE OF BLEACHING

The bleaching results are not permanent. Over time, the bleaching effect has a color relapse. It has been estimated, that after 3 years of the end of the bleaching treatment, 66% of the bleached teeth have a certain degree of "color relapse" [2]. This relapse is called "secondary dental discoloration" and varies while it is not predictable. In general, the more difficult the bleaching effects, the more likely a relapse to be detected [105]. The causes of the secondary dental discoloration can be a reproduction of the oxidized discolored molecules and the possible increase in permeability that allow extrinsic stains to "re-color" the teeth [106].

It is intresting to mention that in a recent clinical study, tooth bleaching with 10% CP in smokers was documented as to be equal to that of non smokers after one year and after removing the superficial stains of smoking and diet [107] thus suggesting that smoking is not actually a contraindication to effective tooth bleaching. In two more studies, patients bleached with 10% CP and 15% HP in six months [108] and with 6% HP with or without 2% nano-hydroxyapatite (n-HA) in nine months [109], were re-examined and degradation of the initial bleaching effect was also observed. Despite this fact, the final result was still significantly better than the tooth color before treatment. Generally, for elongating the bleaching maintenance period, a repeating application of a mild agent (10% CP with trays at-home should be suggested once per year-1/2 syringes of 1.2-1.5 ml).

DISCUSSION

Evidence-based data of the relevant literature, suggest that tooth bleaching is safe and can be attempted under specific conditions. Of outmost importance are: a) the proper selection of case, b) use of mild bleaching protocols, particularly in young patients, c) well-informed patients, d) application of specific protocols for at-home and in-office techniques, e) frequent recall appointments, and f) informed dentist on new research findings.

From peroxides, the carbamide peroxide is expected to cause milder reactions both at local and systemic level, because of its gradual decomposition into hydrogen peroxide (and urea). For this reason, hydrogen peroxide is proposed to be used only in-office while carbamide peroxide only at-home.

Dentist's role in the bleaching procedure is that of the coordinator of the composition, time and way of application of the various materials according to each specific case. A well-informed patient is a good subject to either fulfill the procedure and/or attract more patients in the clinic. Naturally, in a dental procedure that the result cannot be guaranteed, an information/consent form should always be signed among relevant parties.

In Europe the treatment of chemically assisted bleaching costs approximately 70-180 euros per dental arc, without specifying, however, whether the bleaching agent is included (and for how many days of use). In Greece of 2015, during the ongoing economic crisis, prices per dental arch ranging double or triple the cost of the bleaching agent keeping the procedure among the expensive ones. It is not clarified however, whether the cost of the bleaching agent is also included. It seems though that the cost of in-office sessions, as well as the cost of material for thirty days is calculated separately.

The new dentist should clarify that mild at-home and in-office bleaching protocols of low concentration and elongated period of application are as effective as the aggressive ones (higher concentrations, repeating sessions, use of bleaching units). These protocols not only maintain great efficiency but they are characterized by fewer side effects.

It is thus extremely important for anyone performing in this field to check often on European and International guidelines and to be regularly informed for relevant changes in legislation. Despite all European guidelines though that permit the use of only up to 16% carbamide peroxide, Greek online and international market is still flooded with peroxides of higher concentrations. Furthermore, there are cases of improvised personalized mixtures of peroxides, which many private dentists prefer, in order to reduce the overall cost. This fact is not easily detected and may lead to unpleasant consequences and extensive decalcification of tooth enamel, a case which enhances false public impressions that "bleaching destroys tooth enamel". For all these reasons,

careful selection of the case, material and technique is of outmost importance. Following instructions, bleaching is absolutely safe and contributes to a final beautiful smile.

CONCLUSIONS

1. Tooth bleaching is a widely used method of improving tooth color.
2. Bleaching is an absolutely safe procedure considering that case, material and technique selection is carefully made.
3. Bleaching materials can be used under supervision at-home, in-office or with a combined technique (at-home and in-office) and without supervision with OTC products.
4. OTC products have pharmaceutical origin and are not clinically tested for elongated periods of use. Caution should be taken when used for elongated periods of time.
5. At-home and in-office bleaching are performed with the application of peroxides and they are used either separately or combined. All techniques arrive at equal bleaching effects. The combined technique has though the lowest relapse and fastest achievement of the bleaching effect.
6. Maintenance of the bleaching effect is not affected by smoking.
7. Hypersensitivity and irritation of the soft tissues are the most common side effects of bleaching procedures. The symptoms however are totally reversible after 24 hours to a week, depending on its extent.
8. Color relapse can be observed gradually and secondary application of 10% carbamide peroxide can be applied once per year for maintenance of the bleaching effect.

ACKNOWLEDGEMENT

A more extended version of this article is published in Greek, in the Hellenic Stomatological Review.

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