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Review Article

Allergenic exposure potential and residual monomer release from implant provisional polymeric materials after static extraction and thermocyclic aging: a narrative review

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Abstract

Implant-supported provisional restorations preserve function, esthetics, occlusal stability, and peri-implant soft tissue architecture before definitive rehabilitation. These restorations are commonly fabricated from PMMA/PEMA resins, bis-acryl composites, CAD/CAM-milled polymers, and additively manufactured resins, all of which may release residual methacrylate monomers into the oral environment. This release may be especially relevant around implants, where peri-implant mucosal tissues differ from periodontal tissues in vascularization, connective tissue organization, and biologic sealing. Static extraction protocols provide reproducible baseline data, but they incompletely reproduce intraoral conditions involving thermal fluctuation, water sorption-desorption, salivary interaction, and physicochemical aging. The aim of this narrative review is to examine the limitations of static ISO-oriented extraction models for evaluating residual monomer release from implant provisional polymers and to assess the role of thermocycling as a complementary dynamic aging model for peri-implant chemical exposure.

Keywords

CAD/CAM PMMA; methacrylate sensitivity; peri-implant mucosa; thermocycling; ISO extraction

Introduction

Implant-supported provisional restorations have moved beyond the role of temporary functional substitutes. In contemporary implant prosthodontics, they contribute to emergence-profile shaping, peri-implant soft tissue stabilization, and transfer of mucosal contours to the definitive restoration. Direct registration of peri-implant soft tissue forms is clinically relevant for preserving tissue architecture [1], while the esthetic biological contour concept emphasizes emergence-profile design in implant restoration [2]. Digital protocols have strengthened this approach by enabling individualized emergence profiles

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and customized provisional restorations with greater reproducibility [3,4].

The material basis of provisional restoration has also changed. Conventional chairside and laboratory-processed resins now coexist with CAD/CAM-milled and 3D-printed polymeric systems. CAD/CAM interim restorations differ from conventionally produced restorations in clinically relevant parameters [5], and direct chairside and digitally fabricated temporary crowns also show technique-dependent differences [6]. Fabrication technique is now a central variable influencing interim fixed dental prostheses [7]. However, mechanical accuracy or digital workflow advantage does not automatically imply biological inertness.

Residual monomer release is therefore central to the evaluation of provisional polymeric materials. Conventional self-curing resins may show cytotoxicity in vitro.[8], and residual monomer content remains a recognized limitation of PMMA-based materials [9]. Importantly, cytotoxicity as a general endpoint does not identify the underlying mode of cellular injury. Dental polymer eluates may induce apoptosis, necrosis, or a mixed response, with potentially different implications for local tissue inflammation. Kansu et al. [10] reported a greater necrotic component with the conventional PMMA denture-base materials evaluated in their study and relatively more apoptosis with alternative materials marketed as hypoallergenic. More recent evidence in human gingival fibroblasts has demonstrated predominantly apoptotic responses with some PMMA-based dental materials [11], whereas other investigations found no detectable apoptosis or necrosis with certain CAD/CAM PMMA polymers [12]. Taken together, these findings indicate that the type and magnitude of cell death depend on the individual formulation, manufacturing route, polymerization efficiency, released concentration, exposure duration, and cellular model rather than on the PMMA classification alone. Although these studies did not directly evaluate thermocycled implant provisional restorations, they demonstrate why cell viability measurements alone provide an incomplete assessment of biological response. Bis-acryl and resin-based provisional materials introduce dimethacrylate compounds such as Bis-GMA, UDMA, and TEGDMA. Study setup, detection strategy, and quantification strongly affect interpretation of monomer-release data [13], while temporary crown and bridge materials show formulation-dependent release profiles [14]. CAD/CAM-milled materials are expected to show lower residual monomer content because of industrial polymerization, but modern leaching studies indicate that they should not be treated as chemically inert without analytical confirmation [15,16].

The implant environment gives this problem a specific biological dimension. Peri-implant mucosal tissues differ from periodontal tissues around natural teeth. Consensus reports define peri-implant health and mucositis within a tissue environment with distinct structural and inflammatory features [17,18,19], while recent reviews highlight connective tissue organization, vascular support, and the implant–mucosa interface [20,21]. These features do not mean that every released compound produces pathology, but they justify focused consideration of prolonged chemical exposure around implant-supported provisionals. This is particularly relevant for methacrylates with documented biological activity. TEGDMA and Bis-GMA have been associated with oxidative stress and altered inflammatory behavior. [22]. At the molecular level, methacrylate exposure may disturb intracellular redox homeostasis through glutathione depletion and increased generation of reactive oxygen species, with downstream effects on mitochondrial integrity and DNA-damage responses involving p53 [23]. NF-κB signalling should not, however, be interpreted as a uniformly activated pro-inflammatory pathway, since its response to dental methacrylates may be cytoprotective, suppressed, or unchanged depending on the monomer, concentration, material formulation, cell type, and inflammatory context [24,25]. This variability is illustrated by Elçi et al. [25], who found that four methacrylate-based gingiva-coloured indirect composite resins maintained cell viability above the accepted cytotoxicity threshold and did not significantly increase apoptosis, necrosis, or TP53 expression in human gingival fibroblasts; NF-κB expression was reduced with only one of the tested materials. These findings indicate that monomer composition alone is insufficient to predict biological performance, which also depends on polymerization efficiency, network stability, the amount of elutable components, and the conditions and duration of exposure. Methacrylate-related contact allergy remains clinically relevant in susceptible patients [26,27]. In this review, allergenic exposure potential does not imply proof of clinical allergy or sensitization; it refers to the capacity of a material to increase local exposure to compounds with irritant or sensitizing relevance.

Most assessments of chemical release rely on static extraction models. These protocols provide controlled baseline conditions, but they simplify the oral environment. Their interpretation is influenced by experimental design [13], and extraction medium, duration, and analytical approach affect measured release [28]. Thermocycling addresses one clinically relevant dimension of oral dynamics: repeated thermal fluctuation. It can affect monomer release from resin composites [29], influence conversion-related resin behavior [30], and forms part of the broader need for standardized artificial aging protocols [31]. Accordingly, the aim of this narrative review is to examine the limitations of static ISO-oriented extraction models for evaluating residual monomer release from implant provisional polymers and to assess the role of thermocycling as a complementary dynamic-aging model for peri-implant chemical exposure.

Implant provisional polymeric materials and residual monomer release

Provisional polymeric materials should not be treated as chemically uniform simply because they serve a similar temporary prosthetic function. Their release behavior depends on polymer chemistry, manufacturing pathway, degree of conversion, porosity, water sorption, and post-processing. Contemporary interim fixed prostheses include conventional acrylic resins, bis-acryl composites, CAD/CAM-milled polymers, and additively manufactured systems, each with different clinical and chemical characteristics [7,32,33].

Conventional PMMA- and PEMA-based materials remain widely used because they are inexpensive, repairable, and familiar in clinical workflows. Their main biological limitation is incomplete polymerization and persistence of residual monomer. Residual monomer content remains an important determinant of PMMA resin behavior [9], while self-curing temporary crown resins may show cytotoxicity in vitro [8]. Water sorption and solubility further contribute to release: fast-polymerizing acrylic resins show monomer release associated with sorption and solubility [34], and PMMA-based systems demonstrate relevant water sorption behavior [35]. These findings support the mechanism by which water uptake facilitates diffusion of residual components from methacrylate polymers.

Bis-acryl provisional materials were introduced partly to overcome the handling, shrinkage, and exothermic disadvantages of conventional acrylic resins. Their matrix contains dimethacrylate monomers such as Bis-GMA, UDMA, and TEGDMA rather than MMA alone. This improves several clinical characteristics but does not eliminate elutable components. Monomer elution from provisional composite materials has been documented [36,37], and elution behavior remains relevant in direct composites for provisional restorations [38]. The issue is not only residual monomer, but also the biological profile of the released compounds, since TEGDMA and Bis-GMA have been associated with cellular stress and inflammatory effects [22,39].

Digitally manufactured materials have changed expectations regarding provisional restorations. CAD/CAM-milled PMMA blocks are industrially polymerized under controlled conditions, generally leading to higher conversion, structural homogeneity, and lower residual monomer content than chairside autopolymerizing systems. CAD/CAM resins may show lower residual monomer content and favorable mechanical properties compared with heat-cured materials [15], and modern leaching analyses support differences between CAD-milled, printed, heat-processed, and autopolymerizing resin systems [16]. Nevertheless, lower release is not equivalent to absence of release.

Additively manufactured provisional resins require separate consideration. Layer-by-layer polymerization is affected by print orientation, post-curing, resin formulation, and surface finishing. Print orientation can influence sorption, solubility, and monomer elution in 3D-printed resin materials [40], while 3D-printed temporary restorative resins may show cytotoxicity in vitro [41]. Studies comparing milled, printed, and conventional provisional materials indicate that additive manufacturing may offer technical advantages but also introduces distinct surface, mechanical, and biological variables [33, 42-45]. Formulation and post-processing remain critical determinants of 3D-printed provisional crown and bridge performance [46].

Thus, residual monomer release is a class-dependent and process-dependent phenomenon, not a marginal issue limited to older acrylic materials. For implant provisionalization, this matters because the material is a polymeric interface exposed to saliva, temperature fluctuation, water uptake, and prolonged soft tissue contact.

Peri-implant exposure and limitations of static extraction

The relevance of residual monomer release becomes more specific in implant-supported restorations. Around natural teeth, restorative materials relate to a periodontal unit that includes cementum, a vascular periodontal ligament, and a specialized dentogingival attachment. Around implants, the biological interface is different. Consensus reports define peri-implant health and mucositis within a tissue environment lacking periodontal ligament attachment and relying on a distinct mucosal seal around transmucosal implant or prosthetic components [17-19]. This does not make peri-implant tissues pathologically weak, but it changes how chemical exposure should be interpreted. The peri-implant mucosa has connective tissue organization and vascular patterns that differ from those around natural teeth. Peri-implant mucosal attachment has been described as a specialized but structurally limited soft tissue barrier [20], and peri-implant soft tissue structure is closely related to biological function [21]. Histological reviews further support differences in collagen fiber arrangement and vascular supply compared with periodontal tissues [47]. These features matter because clearance, repair, and inflammatory containment depend partly on vascularity and connective tissue organization. Implant-supported provisionals are deliberately used to shape tissue, not merely to occupy prosthetic space. They guide emergence-profile conditioning and mucosal contours during healing, as shown in clinical and digital workflows for individualized implant profiles [1-4]. This prolonged contact exposes the peri-implant mucosa not only to restoration geometry, but also to surface chemistry and diffusible components released during aging. Material-dependent effects on peri-implant soft tissues have been reported [48,49], supporting the view that clinical suitability cannot be judged only by fit, strength, esthetics, or fabrication convenience.

Static extraction models remain essential because they provide controlled and reproducible conditions for evaluating substances released from polymer-based materials. ISO 10993- and ISO 7405-oriented approaches

remain important in cytotoxicity and chemical safety assessment of dental materials [50]. Their limitation is not lack of rigor but restricted ecological completeness. Static extraction describes release under defined laboratory conditions, while the oral environment includes thermal shifts, water uptake, salivary contact, pH variation, and progressive aging.

Methodological choices strongly influence static extraction data. Monomer-release results are shaped by extraction conditions, detection method, specimen preparation, and quantification strategy [13], and experimental heterogeneity remains a major limitation when comparing released components from dental resin-based materials [51]. The extraction medium also affects release: saturation conditions can reduce in vitro leakage of monomers from composites [52], and immersion medium, duration, and analytical design influence measured concentrations [28].

Therefore, static extraction does not reveal an absolute biological property of a material, but its behavior under a defined scenario. This limitation is relevant for implant provisionals, which may remain in function for weeks or months in close contact with peri-implant tissues. Water sorption can modify diffusion pathways and facilitate release of residual components [34,35], while provisional crown and bridge materials differ in fluid absorption over time [53]. Porosity, sorption, and solubility further support the role of water-mediated changes in acrylic and resin-based dental polymers [54,55]. A material that releases low monomer levels during constant-temperature immersion may behave differently after thermal expansion and contraction, sorption-desorption, and surface degradation. Thermocycling can influence monomer release from resin composites [29], and thermal cycling may affect degree of conversion and related resin behavior [30].

Static extraction can identify and quantify released components, but it cannot independently determine tissue-level relevance. The same concentration may have different implications depending on exposure duration, clearance, permeability, and whether the exposed interface is periodontal or peri-implant. This matters because Bis-GMA and TEGDMA have documented cytotoxic, irritant, or sensitizing relevance [22,39], and clinical data support methacrylate exposure relevance in susceptible individuals [26,27]. Static ISO extraction should therefore be understood as the first layer of assessment rather than the final representation of intraoral exposure.

Thermocycling as a dynamic oral simulation model

Thermocycling is widely used to simulate repeated thermal fluctuations experienced by dental materials intraorally. Its value is not that it reproduces the entire oral environment, but that it isolates one clinically important stressor: recurrent transition between cold and hot conditions. For provisional polymers, this is relevant because temperature variation may affect the material surface and internal network through expansion, contraction, water movement, and fatigue-like processes. Artificial aging protocols must therefore be standardized carefully if they are to provide clinically meaningful information rather than merely accelerated degradation [31]. The commonly used range of approximately 5°C to 55°C approximates thermal extremes generated by cold and hot food or beverages. However, the meaning of thermocycling depends on protocol design. Cycle number, dwell time, transfer time, storage medium, and specimen geometry can substantially affect interpretation of aging outcomes [31]. Thermocycling is scientifically useful only when controlled, transparently reported, and interpreted as a model of thermal stress rather than a complete replica of intraoral function. Thermocycling may influence residual monomer release through several mechanisms. Repeated thermal expansion and contraction can generate internal stress within polymer networks, particularly in materials with heterogeneous phases, filler–matrix interfaces, or incomplete conversion zones. Thermal cycling or staining media can alter surface and physicochemical properties of dental materials [57], while thermocycling affects physical properties and biocompatibility-related parameters of CAD/CAM restorative materials [58]. Such changes are relevant because diffusion is governed not only by initial composition, but also by evolving accessibility of residual components inside the polymer matrix.

Water movement is another major mechanism. During thermocycling, polymers are repeatedly exposed to aqueous media at changing temperatures, which may intensify sorption-desorption. Thermocycling can influence water sorption and solubility in 3D-printed and conventional denture-base materials [55]. Water uptake may plasticize methacrylate polymers, increase intermolecular spacing, and facilitate diffusion of low-molecular-weight substances. Similar relevance of water sorption has been demonstrated in provisional crown and bridge materials [53] and acrylic or PMMA-based polymers [34,35,54].

A Bulgarian-led comparative study of 3D-printed, CAD/CAM-milled, and conventional PMMA denture-base polymers subjected to artificial aging similarly demonstrated that sorption behavior depends on both the material and manufacturing route [56]. Although denture-base polymers cannot be considered direct equivalents of implant provisional materials, these findings further support the material-dependent nature of aqueous aging.

Direct experimental evidence links thermocycling and monomer release. Thermocycling affected monomer release from bulk-fill composite resins [29], and artificial aging may be associated with continued monomer release from composite resins [59]. Thermal cycling may also influence degree of conversion [30], which matters because incomplete conversion remains a principal source of residual monomer availability. These studies do not prove identical behavior for all provisional implant

polymers, but they support the concern that static immersion alone may not capture release kinetics after thermal aging. Thermocycling also changes material properties that may indirectly affect chemical release. Thermal cycling can alter surface roughness, hardness, and flexural strength of denture resins [60]; immersion and thermocycling in beverages can affect resin composite roughness [61]; and coffee thermocycling may alter color and translucency of milled and 3D-printed materials [62]. These properties are not equivalent to monomer release, but surface degradation, roughness, and altered bulk stability may increase effective contact with the medium and facilitate diffusion. The relevance of thermocycling is particularly strong for digitally manufactured provisional materials. CAD/CAM-milled polymers benefit from industrial polymerization, but aging can still modify their physical and chemical behavior. Thermal cycling influences microhardness of CAD/CAM materials [63], and broader analyses show effects on physical and biocompatibility-related parameters [58]. Additively manufactured resins introduce variables including print orientation, post-curing, and resin formulation. Print orientation directly affects sorption, solubility, and monomer elution in 3D-printed resin materials [44], while thermal aging affects the physico-mechanical behavior of experimental 3D-printed denture-base resin composites [64].

Comparative studies further suggest that manufacturing route influences aging behavior. Additive, subtractive, and conventional techniques produce different provisional-material performance profiles [65]. Manufacturing method has been linked with monomer release, cytotoxicity, and surface roughness in temporary fixed prosthetic materials [43], and conventional, milled, and 3D-printed provisionals differ in mechanical and surface properties [33]. Temporary and permanent 3D-printed crown and bridge resins also differ in characterization profiles [45]. Dynamic aging may therefore interact with manufacturing technology, so performance cannot be inferred from category labels alone.

Thermocycling should be understood as complementary to, not a replacement for, static ISO extraction. Static extraction provides baseline chemical information; thermocycling tests whether this baseline changes under repeated thermal and aqueous stress. Aging procedures can affect monomer release, sorption, surface properties, and mechanical behavior in ways not reducible to initial composition alone [29,37,57,59]. Thermocycling does not reproduce mastication, biofilm, enzymatic degradation, salivary renewal, or full pH variation; acidic exposure [66] and mechanical loading [67] may act through additional degradation pathways. Nevertheless, thermocycling challenges polymer networks in a way that constant-temperature immersion cannot and may reveal exposure patterns more relevant to provisional implant polymers than static extraction alone.

Clinical implications and future directions

The clinical relevance of residual monomer release from implant provisional materials lies in the relationship between material-derived exposure, duration of tissue contact, and host susceptibility. Provisional restorations are often evaluated according to fit, fracture resistance, esthetics, surface quality, and ease of fabrication, but their biological behavior is equally important during prolonged contact with peri-implant tissues. Long-term temporary restorations have recognized clinical utility [68], yet prolonged use increases the time during which residual monomers or degradation products may interact with oral tissues.

Methacrylate monomers are not biologically inert. Dental resin components have been associated with cytotoxicity, oxidative stress, and altered cellular responses [8,22,39,69]. TEGDMA and Bis-GMA may influence neutrophil behavior rather than acting only as passive chemical residues [22], and contact allergy to dental materials, including methacrylate reactions, remains relevant in dental patients [26,27].

Bulgarian clinical observations have further shown that methacrylate hypersensitivity may occur without pathognomonic intraoral findings, emphasizing that suspected reactions require interpretation through exposure history and appropriate allergy testing rather than mucosal appearance alone [70]. Release of MMA, Bis-GMA, TEGDMA, or related compounds should therefore be interpreted as biologically meaningful exposure, even when it does not directly prove clinical allergy. Material choice has practical implications. CAD/CAM-milled PMMA materials are often considered more chemically stable, with studies supporting reduced monomer leaching compared with conventional autopolymerizing systems [15,16], but they should not be described as risk-free. Additively manufactured resins may show release behavior influenced by print orientation, post-curing, and formulation [40,45,46], while conventional PMMA/PEMA and bis-acryl materials differ in residual monomer profile and biological behavior [9,14,34,36]. Patients with contact allergy, unexplained mucosal reactions, peri-implant inflammatory susceptibility, or known sensitivity to acrylates and methacrylates may benefit from cautious material selection. If thermocycling reveals increased monomer release compared with static extraction, this does not automatically translate into clinical hypersensitivity, but it may indicate a higher methacrylate exposure burden under conditions closer to oral thermal stress.

Future research should combine standardization with greater ecological relevance. Static extraction remains useful as a baseline method, but should be paired with dynamic aging models when materials are intended for prolonged intraoral use. Artificial aging protocols require clearer harmonization of cycle number, dwell time, medium, specimen geometry, and aging sequence [31].

Comparative protocols should apply static ISO-oriented extraction and thermocyclic aging to the same material groups under clearly defined conditions. Since study setup, detection method, and quantification strategy strongly influence monomer-release data [13], future studies should report material composition, specimen dimensions, finishing, post-curing or polymerization conditions, extraction medium, storage time, and analytical limits of detection.

Analytical methodology also requires refinement. HPLC remains widely used for quantifying residual monomers [71,72], LC-MS/MS may provide greater specificity for Bis-GMA and BPA-related derivatives [73], and GC-MS remains relevant for volatile and semi-volatile compounds, particularly MMA and related methacrylates. [74,75]. Chemical detection alone is insufficient to establish the biological relevance of released monomers. Future protocols should therefore combine quantitative chemical analysis with tissue-relevant biological endpoints, including cell viability, apoptosis and necrosis [10-12], oxidative-stress markers, inflammatory mediator release, and selected cellular stress-response pathways such as NF-κB and p53 [23-25]. These endpoints should be assessed under matched static-extraction and thermocyclic-aging conditions, using defined eluate concentrations and exposure periods. Such an integrated approach would distinguish the identification and quantity of released compounds from their actual biological effects and would provide a more clinically meaningful assessment of implant provisional polymeric materials.

Conclusion

Residual monomer release from implant provisional polymeric materials is influenced by material formulation, polymerization efficiency, manufacturing route, water interaction, and aging conditions, and therefore cannot be predicted from the material category alone. Static ISO-oriented extraction provides reproducible baseline information but it does not capture changes in chemical release that may occur during repeated thermal and aqueous aging. Thermocycling is best regarded as a complementary model for determining whether aging alters the release profile of provisional polymers rather than as a replacement for static extraction or as direct evidence of clinical toxicity or hypersensitivity. A clinically meaningful assessment should therefore combine chemical analysis after static and dynamic aging with tissue-relevant biological endpoints, particularly when prolonged implant provisionalization or known methacrylate sensitivity is present.

Additional information

Ethical compliance

The authors declared that no clinical trials were used in the present study.
The authors declared that no experiments on humans or human tissues were performed for the present study.
The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.
The authors declared that no experiments on animals were performed for the present study.
The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

Conflict of interest

The authors declare that they have no conflict of interest and no affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

Author contributions

Conceptualization: D.R. and M.D.
Methodology: D.R., V.M.T., I.G., and M.D.
Literature search and investigation: D.R., V.M.T., and Y.T.
Resources: D.R., V.M.T., I.G., R.G.U, V.L., R.A., and M.D.
Formal analysis and critical synthesis: D.R., V.M.T., R.G.U, V.L., R.A., and M.D.
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