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## REVIEW

# Opinions from five oral specialists on 3D printing in the challenge of customized oral healthcare. What can plasma technology bring?

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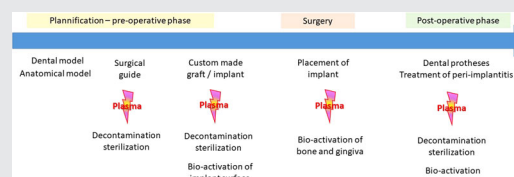
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## Abstract

The field of “plasma medicine” is expanding. It is based on advances in plasma physics and chemistry; a better knowledge of the species produced, a better control in the creation of gaseous plasmas, enable different plasma processes with potential different clinical applications. In the medical field, progress is being made towards predictive, preventive, personalized, participatory, and populational medicine. In particular, three-dimensional printing is useful in the challenge of customized oral healthcare. For example, plasma technology offers many options to optimize the use of custom-made prosthesis, particularly in the area of oral medicine and oral surgery.



## KEYWORDS

oral medicine, oral surgery, plasma medicine

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Today's medicine tends to be defined as predictive, preventive, personalized, participatory, and populational.

Personalized, as treatments will be tailored to patients. The replacement of deficient organs or joints or presenting terminal degenerative pathologies is an important therapeutic challenge and can only be envisioned by the manufacture of custom-made prostheses. New biomaterials must also be able to replace a variety of living tissues, in particular for the purpose of filling tissue defects, thus enabling to restore functions. Requirements and specifications for biomaterials to design customized prosthetic parts are complex.

In the field of oral medicine and oral surgery, these new challenges stand at different levels.

One of them concerns complex oral rehabilitation, where dental implants can be used to replace one or more teeth. To be successfully placed in the mouth, a favorable bone and mucous environment is mandatory. It is now possible to accurately determine the shape of the bone defect, its volume and to plan from beginning to end, the necessary bone reconstruction, to ideally position the implant restoring optimal and long-lasting masticatory and esthetic functions. Guided surgery using three-dimensional (3D) printing technology is definitely an indispensable aid and tool.

In this article, we propose four cross-perspectives around the challenges of customized oral healthcare, emphasizing in particular on the contribution of plasma technology in this area (Figure 1).

## 1 | 3D PRINTING IN ORAL HEALTH—HOW DOES IT WORK? WHICH MATERIAL IS USED?

The evolution of 3D printing in dentistry has greatly improved and modified the work-flow for dental practitioners and technicians. Until the emergence of

additive manufacturing processes, digital techniques for designing and manufacturing medical devices for dental use were essentially oriented towards the subtractive manufacturing mode by milling. Initially, the concept of 3D printing was a technology that enabled to create physical objects from a 3D digital file using a computer-controlled nozzle.<sup>[1]</sup> In the last decade, the process, as well as its fields of application and materials available to be printed (ceramics, polymers, metal alloys...<sup>[2]</sup>), has been widely extended. Among the technologies that can be applied for medical use, stereolithography is particularly interesting in terms of product resolution.<sup>[2]</sup> Briefly, it consists of polymerizing a photosensitive liquid resin with an ultraviolet laser, voxel by voxel on each layer of the object to be printed.<sup>[2]</sup> Between each layer, an addition of resin is brought on the top of the printing tray. The layers' precision is lower than 100  $\mu\text{m}$  in thickness.<sup>[3]</sup> Resins used for 3D printing in dentistry are derived from polymethyl methacrylates.<sup>[4]</sup> They are formed by the polymerization of methyl methacrylate monomers according to an addition process following a three-step procedure of initiation, propagation, and termination.<sup>[5]</sup> The printing protocol must thus respect and allow the course of these stages. However, such a technique presents some limitations. These biomaterials comply with European regulations as class IIa medical devices, that is, they can be positioned in the patient's oral cavity, but not implanted as would bone substitutes or titanium implants, for example. This characteristic is partly related to their potential toxicity, which constitutes a wide topic of research in the international literature. In fact, once printed, the dental devices must undergo a double chemical and physical posttreatment procedure to finish the polymerization and reduce the resin risk of toxicity.<sup>[6]</sup> Indeed, poor execution of the protocol can potentially lead to release, into the patient's body, of free monomers left on the surface of the material.<sup>[7]</sup> Recently, Nam et al.<sup>[8]</sup> have pointed out that uncured monomers

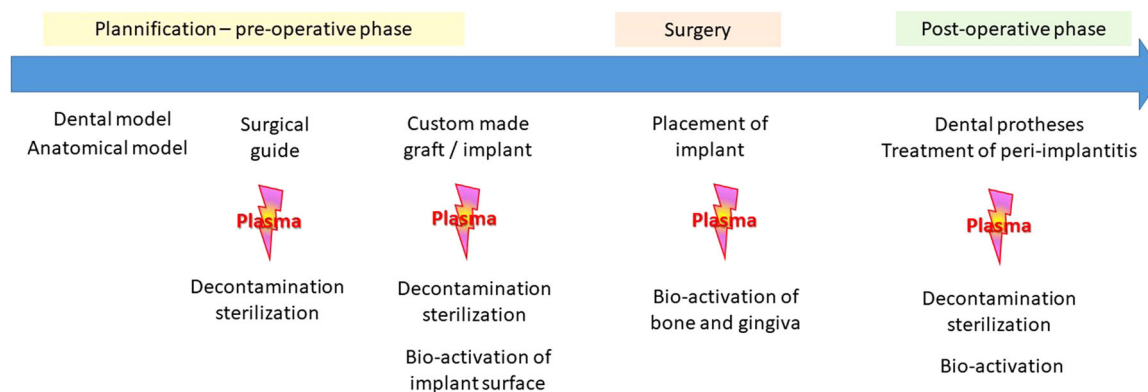


FIGURE 1 Contribution of plasma technology in customized oral healthcare.

but also photoinitiators and additives may be considered toxic elements and should be targeted when post-treatment procedures are designed.

## 2 | 3D PRINTING IN ORAL HEALTH—WHAT ARE THE SURGICAL INDICATIONS?

The market for 3D printing in oral health is growing at an annual rate of 20.2% and is estimated to be worth \$7.9 trillion by 2027, according to a report by a research firm *Markets and Markets*.<sup>[9]</sup> Multiple applications have been developed using rapid prototyping technologies and various materials.<sup>[10]</sup> Once mastered, 3D printing in oral health allows simplification, flexibility, and work-time reduction in producing medical devices. Today, it offers users a growing list of indications, and it can easily be integrated into the workflow of any dental practice or laboratory.<sup>[11]</sup>

To date, in dentistry and oral surgery, the association of intraoral cameras, computer-aided designing, and 3D printing have enabled the development of full digital workflows useful for complex oral rehabilitations.

*Dental models* are used by both the practitioner and the lab technician to analyze, plan implant treatment and fabricate dental prostheses (Figure 2).

For surgery, *anatomical models* can also be printed for preoperative planning in complex cases, that is, for presurgical conformation of osteosynthesis plates<sup>[12]</sup> (Figure 3).

*Surgical guides* are also produced by this technique. They are designed to help the practitioner orient instruments and place implants in a more precise, accurate, and customized way (Figure 4).

Surgical guides are very useful, especially in the management of complex cases: anterior maxillary areas with an important esthetic issue, complex surgical rehabilitation in patients at risk (irradiated field implantology, implant-stabilized maxillofacial prosthesis).

Dental prostheses such as crowns, bridges, overlays, or complete removable prostheses can be printed in resin, metal, or ceramic (Figure 5). This use of technology facilitates the use of materials that would otherwise be difficult to craft and utilize and diminishes the manual, labor-intensive production and postproduction techniques.<sup>[13]</sup> In orthodontics, 3D printing has enabled the development of alignment trays (Figure 6).

Implantology has pushed the boundaries of oral rehabilitation. In complex cases, we can imagine, tomorrow, the use of custom-made implants, adapted to the bone but also the patient's gingival profile.

Also, when necessary, despite the use of custom-made implants, the preimplant bone and gingival tissue layout can be anticipated and planned thanks to 3D technology. Bone grafts can be prepared and milled before insertion into the mouth as well.

## 3 | WHAT CAN PLASMA TECHNOLOGY BRING IN 3D PRINTING FOR MEDICAL APPLICATIONS?

3D printing technology allows the realization of tailor-made, implantable parts, perfectly adapted to the patient. On the one hand, this technology is particularly

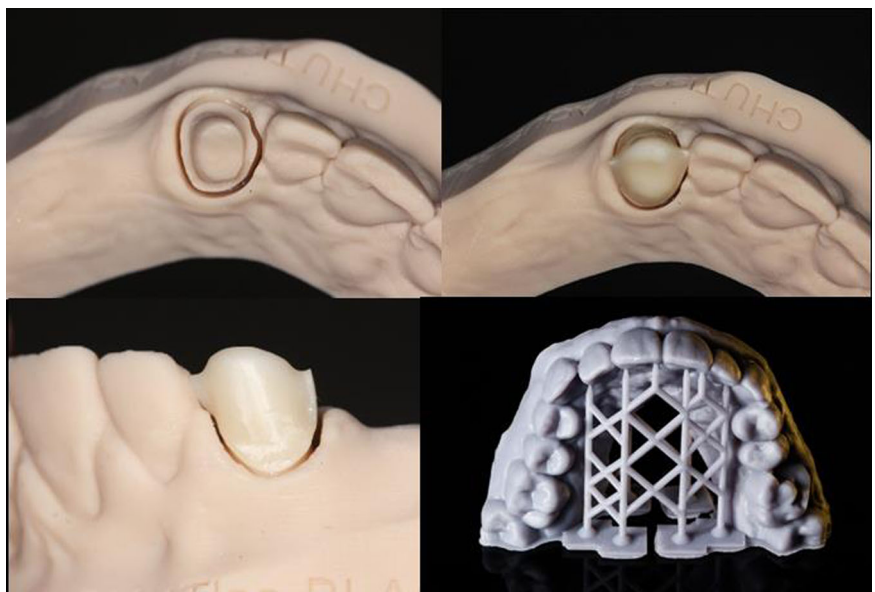
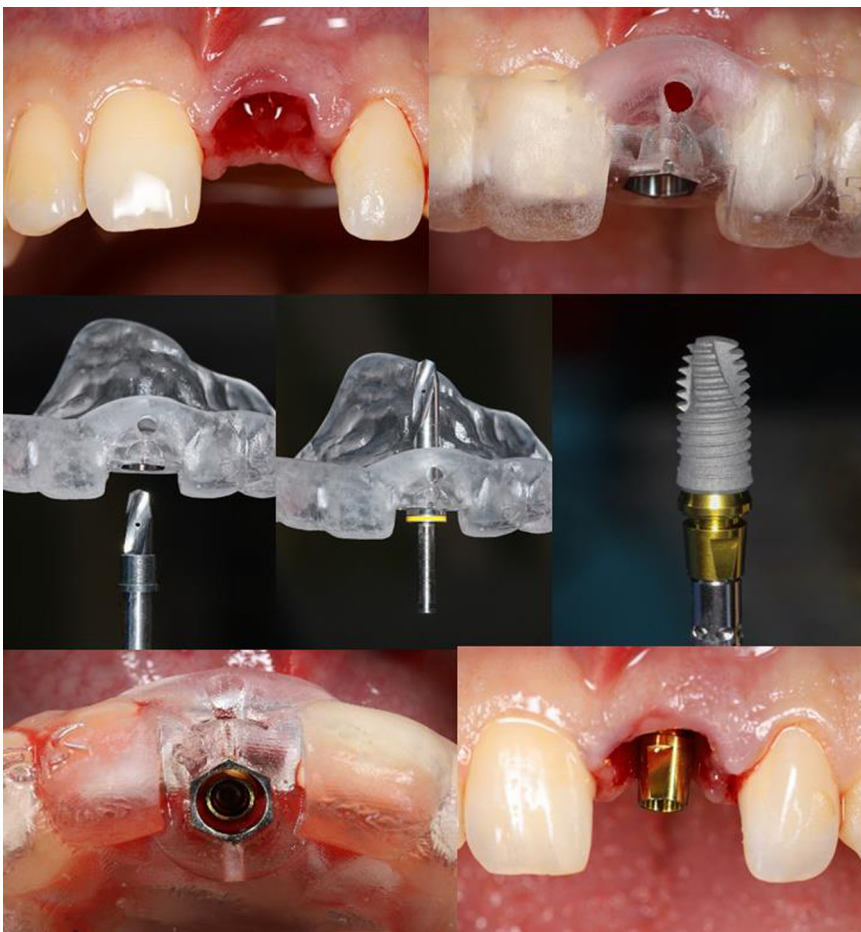


FIGURE 2 Use of 3D printing in the production of dental models and dental prostheses.



**FIGURE 3** Anatomical models printed in a preoperative planning. These models are very useful in the follow-up of complex clinical cases. Here the surgeon can simulate the removal of a mandibular tumor and adapt the plates of osteosynthesis, preoperative. This helps reduce surgical time.



**FIGURE 4** Placement of an implant, in an esthetic area (maxillary). A surgical guide allows a more secure, better-controlled procedure. Surgical time is reduced.



**FIGURE 5** Dental prostheses with 3D printing technology.



FIGURE 6 Orthodontic alignment trays, custom made.

promising and allows new therapeutical alternatives. On the other hand, it deals with new constraints.

- Plasma technology could allow sterilization of printed parts before implantation.

In the medical field, the majority of instrumentation is sterilized by autoclaving, which is a hot and moist treatment. This technology is effective but does not allow for the treatment of “heat sensitive” materials. Low-temperature sterilization techniques are available, most often using gamma, ultraviolet, or ethylene oxide. These processes are sometimes costly and toxic in the case of ethylene oxide. Furthermore, UV sterilization makes it difficult to treat objects of complex shapes. The principle of cold plasma sterilization is therefore a promising alternative. Processes using nitrogen atoms, and thus nonoxidizing, would allow the parts to be sterilized by 3D printing, with thermosensitive materials, and without structural alteration.<sup>[14–16]</sup>

In particular, if 3D printing makes it possible to obtain a personalized prosthesis, perfectly adapted to the clinical situation, it is therefore difficult to accept that the sterilization process induces a dimensional variation of the object. As we previously presented in this article, surgical guides need to be perfectly adapted to the patients to respect the previously established customized treatment plan. The use of nonequilibrium plasma discharge has been studied to remove organic residues from surgical instruments. This method has been shown to be effective and without risk of toxicity.<sup>[17]</sup> The use of cold atmospheric plasmas (CAPs) was described more than 50 years ago. It is not intended to replace standard sterilization processes, but it has its place in the decontamination and sterilization of biocompatible biomaterials or sensitive materials.<sup>[18]</sup> Depending on the conditions of use, some plasma devices avoid the negative effects of thermal loading, however, changes due to plasma interaction cannot be eliminated. They only affect the surface (a few atomic layers) and can even have beneficial effects, but the material influences the plasma composition.<sup>[19,20]</sup> Thus, a standardized low-pressure plasma sterilization process, reproducible photon and particle fluxes will most likely be achieved with pure molecular process gases.<sup>[18]</sup> The use of pure

nitrogen discharge and postdischarge limit the production of UV radicals for example.

Plasma is effective against a broad spectrum of pathogens, including bacterial spores and prions, both of which display a high level of resistance to chemical and physical treatments.<sup>[15,21]</sup>

The antimicrobial and surface modification potential of plasma demonstrated in *in vitro* and *in vivo* models would suggest CAP as a promising option in the treatment of contaminated titanium implants (e.g., peri-implantitis).<sup>[22,23]</sup>

Furthermore, the use of plasma on the titanium surface has shown beneficial effects with an increase in bone formation around titanium biomaterials. This is explained by the modifications of the surface state and in particular the wettability and the reduction of reactive oxygen species.<sup>[24,25]</sup>

- Plasma technology could allow surface treatment of printed parts, peroperative

Surface modifications by plasma treatment, at atmospheric pressure, at room temperature, in a care unit, and for example in the operating room are interesting prospects. Thus, during the procedure, the surfaces of printed prostheses could be treated for decontamination, or activated.

The change in wettability of plasma-treated surfaces is known. Various studies show that treatment with CAP can improve or slow down cell colonization.

Plasma technology could potentiate osteointegration for example. This further increases the therapeutic possibilities. One of the objectives of using custom-made prosthetic and implantable parts is to be able to push therapeutic limits. Thus, if the plasma technology decreases the duration of the healing phase, potentiates the phase of biointegration (bone and/or mucosa), the success of the rehabilitation is increased. Also, oral microorganisms' adhesion can be reduced by CAP application.<sup>[26,27]</sup> Thus, the materials used in 3D printing could be activated by plasma and plasma technology could render these biomaterials bioactive.<sup>[28,29]</sup>

The modification of the gas or the parameters of the plasma induces the modification of the physicochemical species produced and therefore of the properties of the plasma. The wettability, the surface state, or even surface energy can be modified.<sup>[30–32]</sup>

The treatment of the bonding interface is a daily challenge in adhesive dentistry. The use of cold plasmas has been widely studied on biomaterials used in dentistry (such as acrylic denture base resin, glass fibers, fiber-reinforced composite posts, and ceramics).<sup>[33]</sup> An increase in bond strength has been demonstrated in the short and long term.<sup>[34]</sup>

In oral surgery and implantology, the use of biomaterials is widely found. Titanium is common

practice. The success of a dental implant is linked to the achievement of implant osteointegration but also to a perfect gingival integration. The surface modification of implants could allow a better biointegration.<sup>[35]</sup> Cold atmospheric plasma is able to increase the wettability of titanium, removing hydrophobic contaminants and forming a thin chemical layer composed of groups like hydroxyl species, thereby producing a more reactive surface.<sup>[36]</sup> Thus, this improves soft and hard tissue healing.<sup>[33]</sup> Reno et al.<sup>[37]</sup> have shown biocompatibility and bioactivity improvement toward osteoblasts and keratinocytes adhesion and proliferation.

These cell adhesion and proliferation properties have also been shown on biomaterials other than titanium, such as certain polymers used in medicine.<sup>[38]</sup> This is enabled by modification of the surface chemistry and morphology, inducing surface cleaning, surface ablation or etching, cross-linking, and modification of chemical properties.<sup>[39]</sup>

## 4 | CONCLUSION

Therapeutic progress is constant and depends on technological progress. Within the framework of “rehabilitation,” esthetic and functional demands are increasingly advanced, and the results are more and more reproducible, reliable, and sustainable. These advances are due in particular to the use of implantable devices tailored to the patient's clinical situation and demands and also the possibility of using precise surgical guides that secure surgical procedures. Plasma technology could provide technological and biological solutions, particularly in terms of sterilization, decontamination, and biological functionalization of printed surfaces (3D printing).

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## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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