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Past, Present, and Future of Soft-Tissue Prosthetics: Advanced Polymers and Advanced Manufacturing

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Millions of people worldwide experience disfigurement due to cancers, congenital defects, or trauma, leading to significant psychological, social, and economic disadvantage. Prosthetics aim to reduce their suffering by restoring aesthetics and function using synthetic materials that mimic the characteristics of native tissue. In the 1900s, natural materials used for thousands of years in prosthetics were replaced by synthetic polymers bringing about significant improvements in fabrication and greater realism and utility. These traditional methods have now been disrupted by the advanced manufacturing revolution, radically changing the materials, methods, and nature of prosthetics. In this report, traditional synthetic polymers and advanced prosthetic materials and manufacturing techniques are discussed, including a focus on prosthetic material degradation. New manufacturing approaches and future technological developments are also discussed in the context of specific tissues requiring aesthetic restoration, such as ear, nose, face, eye, breast, and hand. As advanced manufacturing moves from research into clinical practice, prosthetics can begin new age to significantly improve the quality of life for those suffering tissue loss or disfigurement.

1. Introduction

The transformative role of prosthetics for those suffering tissue loss or disfigurement cannot be understated.[1,2] These personalized treatments restore aesthetics and function to missing or malformed tissue using synthetic materials that mimic the characteristics of natural tissue. Since the first devices fashioned from rudimentary materials, the science and art of prosthetics has significantly progressed. Now, the marriage of advanced manufacturing with sophisticated polymer science promises highly personalized and realistic prosthetics.[3–7] The impact of the advanced manufacturing revolution is significant; traditional labor intensive approaches involving physical casting and hand-crafting[8–10] are being replaced by 3D scanning, computer modeling, and multimaterial 3D printing.[5,11] Although digital technology has been used in prosthetics for the past 30 years,[12,13] it is only the last decade that has seen its rapid development as part of the fourth industrial revolution.[14] This change in practice is evidenced by the significant fraction of recent literature describing advances in 3D printed prostheses, including technological advances[4,15–18] and clinical reports.[19,20] Further innovations involving collaborations between clinicians, academics, and industry, promise even greater capabilities. The future will see 3D printers that can mix materials as desired during fabrication[21] and those that can 3D print organic semiconductors and piezoelectric polymers for sensing and bionics[22–24] (**Figure 1**). This report is focused on polymers for soft tissue, external, personalized, prosthetics with clinical applications for the ear,[25] nose,[26] eye,[27] face,[28] breast,[29] and hand.[30] The characteristics of both traditional and 3D printable polymeric materials, as well as current advanced manufacturing technologies and those in development, are also reviewed.

The earliest evidence of prosthetics dates back to ≈2300 BC, where Egyptian mummies have been discovered with eye, nose, and genital reconstructions fashioned from plaster packed with mud, sand, linen, butter, or soda (Figure 1).[31] Wood, cloth, natural waxes, resins, and metals were later used as the material of choice for rudimentary prostheses.[32] Prostheses remained relatively unchanged for thousands of years until the 16th century, where prosthetic noses and eyes were made from parchment, wax, wood, hard rubber, gold, silver, and copper.[33] Metals continued as a fundamental material throughout the 19th century, largely due to their ability to be shaped and molded as needed.[34,35] One of the first polymers to be used in prosthetics, poly(methyl methacrylate) (PMMA), was developed in response to the glass shortages in the World Wars of the 20th Century.[36] This polymer went on to become the most common prosthetic material of the time, and still finds use today in artificial eyes[33] and prosthetic substructures.[37] Further innovations in the 20th century produced many new polymers, such as vinyls, copolymers, plastisols, and one of the most significant materials in prosthetics, silicone.[38] Discovered in the early 1900s by Fredrick Kipping, silicone was first used in prosthetics by George W Barnhart in 1960.[39] This versatile polymer remains a primary prosthetic material today due to its soft tissue-like properties, ease of manipulation, chemical inertness, durability, and excellent biocompatibility.[40,41] The search for alternative materials

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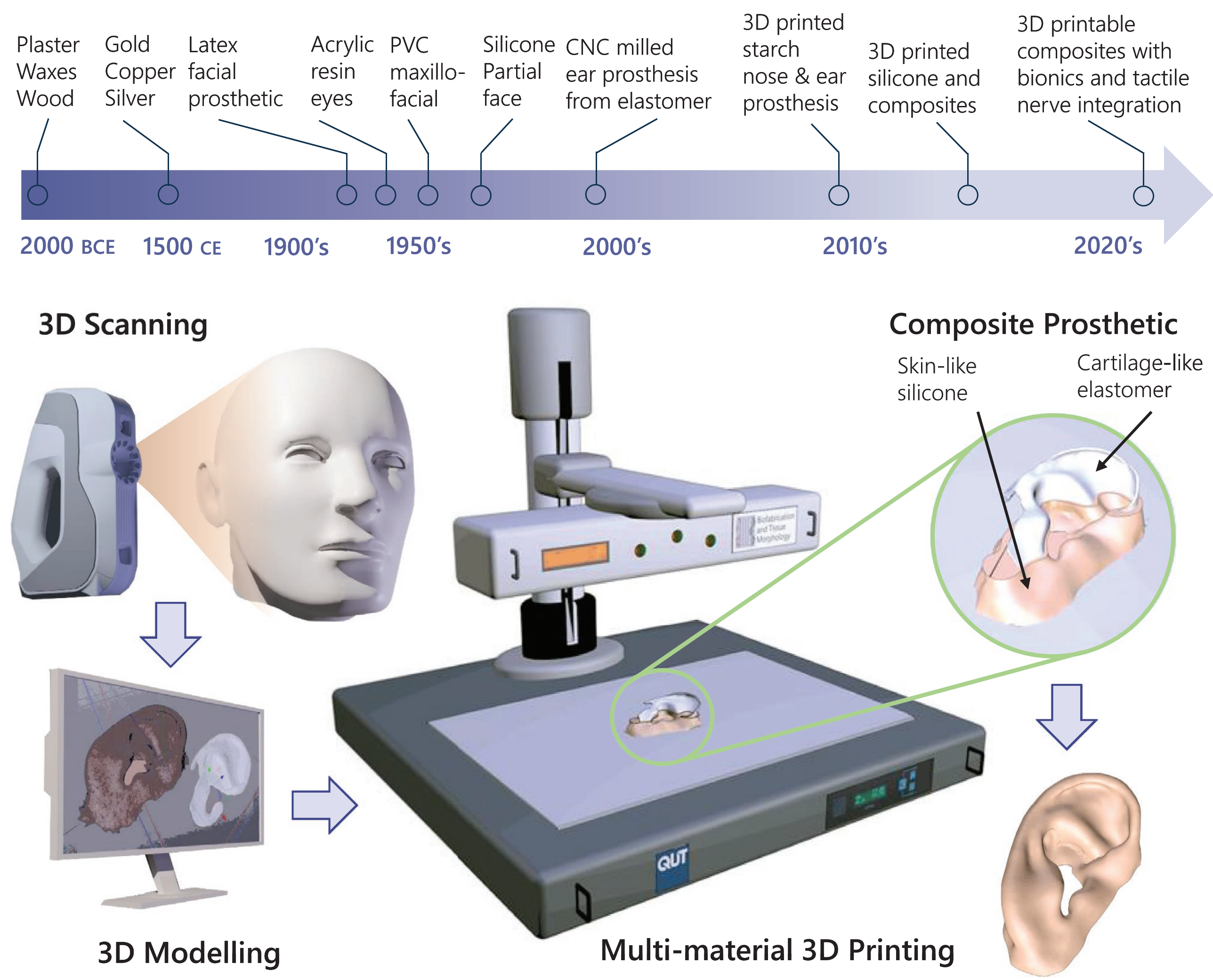

Figure 1. Top: Timeline showing significant innovations in the materials science of prosthetics past, present, and future.[4,18,23,24,31,33,39,92,138,313–315] Bottom: the typical advanced manufacturing pipeline for producing prosthetics. Newer techniques include the ability to fabricate multimaterial prosthetics during the single printing process.

with silicone-like properties led to the development of polyurethane elastomer in the 1970s, however, this was found to be comparatively difficult to process with limited colorfastness.[33]

More recently, innovations in 3D printing have led to the development of new specialized material blends and crosslinking methods, finely tuning their properties to optimize their suitability for 3D printing and thereby enabling a large range of mechanical and visual properties (Figure 1).[21,42] Much of this innovation comes from the 3D printer manufacturers themselves, with materials comprising proprietary blends of polymers suitable for printing only on their machines.[43–47] For example, one of the leading commercial 3D printer companies, 3D Systems (South Carolina, USA), have over 100 different polymers available for their 3D printing technologies; from soft elastomeric polymers to rigid nylons and Acrylonitrile butadiene styrene (ABS).[48] Many of these polymers also contain complex blends of methacrylates, urethanes, and other engineered polymers. The recent introduction of these into to the market and consequent need for clinical development, biocompatibility testing, and regulatory approval, limit their regular clinical use in prosthetics.[49,50] However, some of these advanced polymers have received ISO-10993, USP Class VI or other biocompatibility certification.[51,52] This increases their potential for use in the routine fabrication of soft tissue prosthetics, eventually rendering traditional prosthetic fabrication approaches obsolete.

2. Biomimicry through Synthetic Polymers

The ideal prosthetic should mimic the visual, textural, and mechanical characteristics of missing or damaged tissue, to the extent that it appears as if natural.[53,54] One of the biggest challenges in prosthetics is imitating human skin. Skin comprises several layers; the epidermis which acts as an outer barrier and produces tone, the dermis which contains connective tissue, hair follicles, sweat glands, and the deeper hypodermis which is also made of connective tissue and fat.[55]

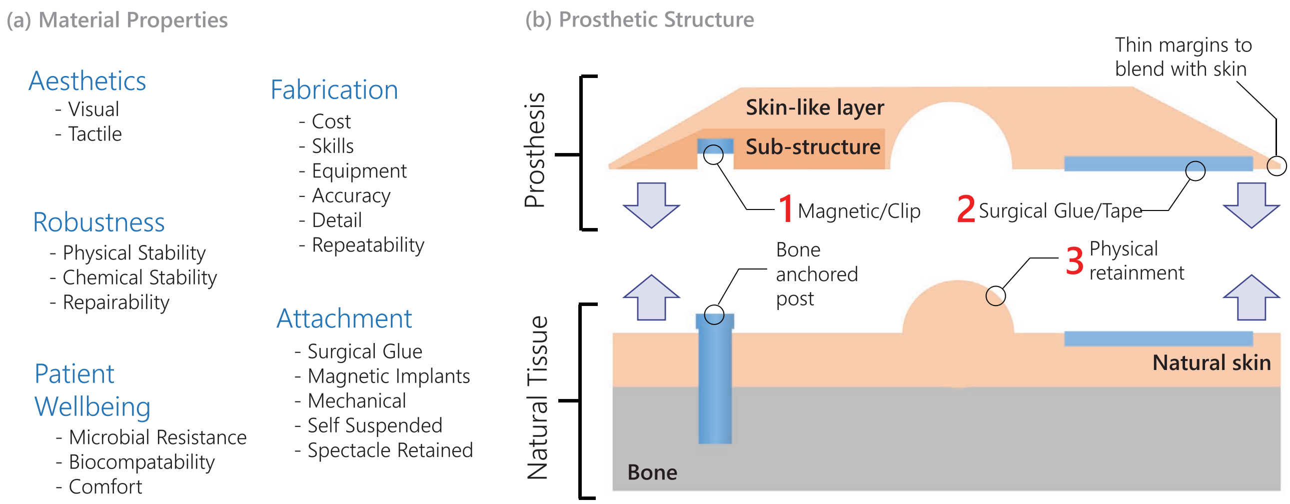

Figure 2. a) Important material properties for polymers in prosthetics. b) Schematic of a typical soft tissue prosthetic including the skin-like layer and substructure. Common patient anchoring approaches are also illustrated, such as: 1) Magnetic/Clip attachment onto osseointegrated attachment posts, 2) surgical glue or tape, and 3) physical retainment onto existing tissue structures or mechanical attachment to glasses frames.

The complex functioning of the various cells, glands, vessels, and follicles within these layers gives skin its diverse properties.[55] Although replicating skin's precise structure is not possible using synthetic polymers, some of its essential characteristics can be reproduced. The fundamental requirements for a successful prosthetic material, summarized in **Figure 2**a, includes aesthetic considerations, such as translucency and texture,[56] as well as tactile properties such as pliability and softness.[57] It must also be able to be intrinsically stained to match the patients' basic skin tone[53,58] and enable the addition of extrinsic detail, such as capillaries and hair.[59] As prosthetics are rarely worn while sleeping, removal and attachment must be straightforward, but attachment must be sufficient for the prosthesis to remain in place during normal activities without causing damage or harm.[60] Common approaches include the use of adhesives, such as glue or tape,[37,61] mechanical fixing to spectacle frames,[62] hair clips,[63] or rings,[64] and surgically implanted osseointegrated (bone integrated) posts for use with magnetic or clip attachment.[65,66] The suitability of each method depends heavily on clinical circumstances. Adhesion approaches, for example, require careful consideration of the bonding parameters to ensure the prosthetic and patient are not harmed during removal.[67,68] Mechanical attachment methods require a stiff framework to be chemically bonded to the prosthetic material, adding to the complexity of the design.[37,53] Implantation of osseointegrated posts for magnetic or clip attachment offers excellent long-term outcomes, however, it involves surgery[1,65,69] (Figure 2b).

On average, traditionally fabricated implant-retained prosthetics require reconditioning or remaking every couple of years.[70] During this time, they are exposed to difficult environmental conditions, such as sunlight (ultraviolet (UV)) and temperature variations.[71] This can cause stiffening and undesirable changes in appearance.[72] Furthermore, they must be able to withstand large temperature ranges of below freezing and up to 120 °C for sterilization.[73] It is also likely that a prosthetic will be exposed to water, sweat, and saliva during normal use, leading to changes in color and degradation of the polymeric structure.[67,74] Likewise, everyday mechanical properties, such as tensile strength, tear strength, and elongation at break are important, particularly around the thin edges of the prosthetic where it blends with the skin.[53,75,76] Comfort, biocompatibility, and breathability are important[77,78] as is low surface friction to avoid skin irritation.[79–81] Finally, poor surface wettability can lead to microorganism growth and may promote the formation of biofilms that resist disinfection.[82,83] This factor is exacerbated by temperature and humidity conditions at the skin-material interface which may be ideal for the proliferation of bacteria and fungi.[84]

3. From Hand-Crafting to Advanced Manufacturing

As with many industries, the field of prosthetics is being disrupted by advanced manufacturing, with the full impact of this technology on the clinical experience yet to be realized.[5,85,86] Remaining challenges include the need for further biocompatibility certification,[87] the development of improved user-friendly production pipelines (3D scanning, computer modeling, etc.),[88] and the need for more clinical evidence-based studies. Aside from high degrees of personalization and realism, the lower costs of advanced manufacturing compare favorably to traditional methods, which are relatively more labor intensive and require high levels of specialized artistic skill.[89] The automation aspects of advanced manufacturing, through lower costs, also improves patient access to high-quality, realistic, and highly personalized prostheses.[89] Both traditional and advanced manufacturing processes follow the same basic template; acquire patient morphology, model the prosthetic, and fabricate the prosthetic. Traditional approaches begin with acquiring a physical impression of the patient's anatomy (**Figure 3**). In some cases, this may be traumatic for the patient.[90] From this, a mold is produced which forms the basis for hand-sculpting of a prosthetic prototype, usually made of wax.[91] The wax prototype is then used to produce a mold into which the final prosthesis

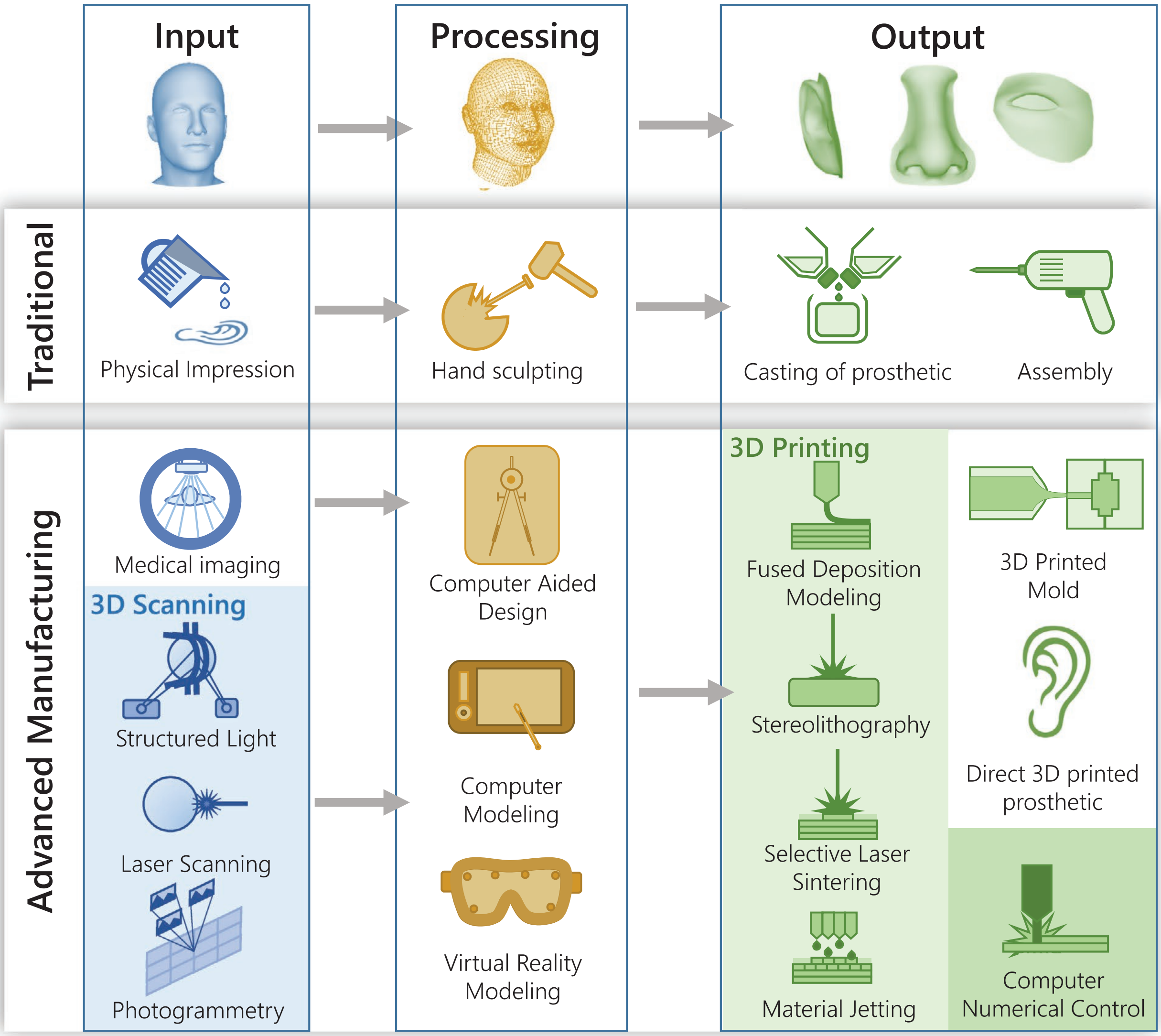

Figure 3. Illustrative map showing both traditional and advanced manufacturing approach for producing a soft tissue prosthetic. The basics steps are input, processing, and output, with 3D printing approaches offering significant advances over traditional methods.

material is cast. Depending on the chosen method, the complexities and details of this process vary widely. For example, room temperature processing is available for some materials enabling the use of dental stone, acrylic, or epoxy molds, whereas, others require high temperatures necessitating more expensive molds and more complex processing.[34,58] Following casting, many prosthetics are hand-painted to add realism, further complicating the materials requirements and contributing to increased labor cost.[53,58,92]

Advanced manufacturing typically begins with medical imaging or 3D scanning in place of the physical casting (Figure 3).[5] This commonly includes scanning the location where the prosthesis will attach, as well as any unaffected contralateral anatomy for use in prosthesis modeling if available.[93] Patient scan data are then transferred to 3D software for the digital design of the final prosthetic. Available software includes engineering-based computer aided design packages (CAD),[94] or polygon-based computer modeling software designed for freeform medical modeling, movies, and animations.[3,95–97] In some applications, advanced modeling software can automate parts of the prosthetic design process,[98] and even simulate mechanical properties prior to fabrication using finite element analysis.[27] The final digital model is then fabricated using computer aided manufacturing approaches; using either subtractive milling methods[99] or advanced manufacturing approaches, such as 3D printing.[100]

Although 3D printing technologies vary in specific details, nearly all use a layer-by-layer approach to build up a 3D object, with each layer comprising a 2D “slice” of the object.[42,101] The particular method used to create each layer determines many of the final material properties of the object. For simplicity, 3D printing methods can be broadly divided into two groups; those which selectively add or extrude material into the object build area, and those which selectively melt (sinter), bind, or polymerize a layer of liquid or powdered material. Six of the most common 3D printing approaches used in

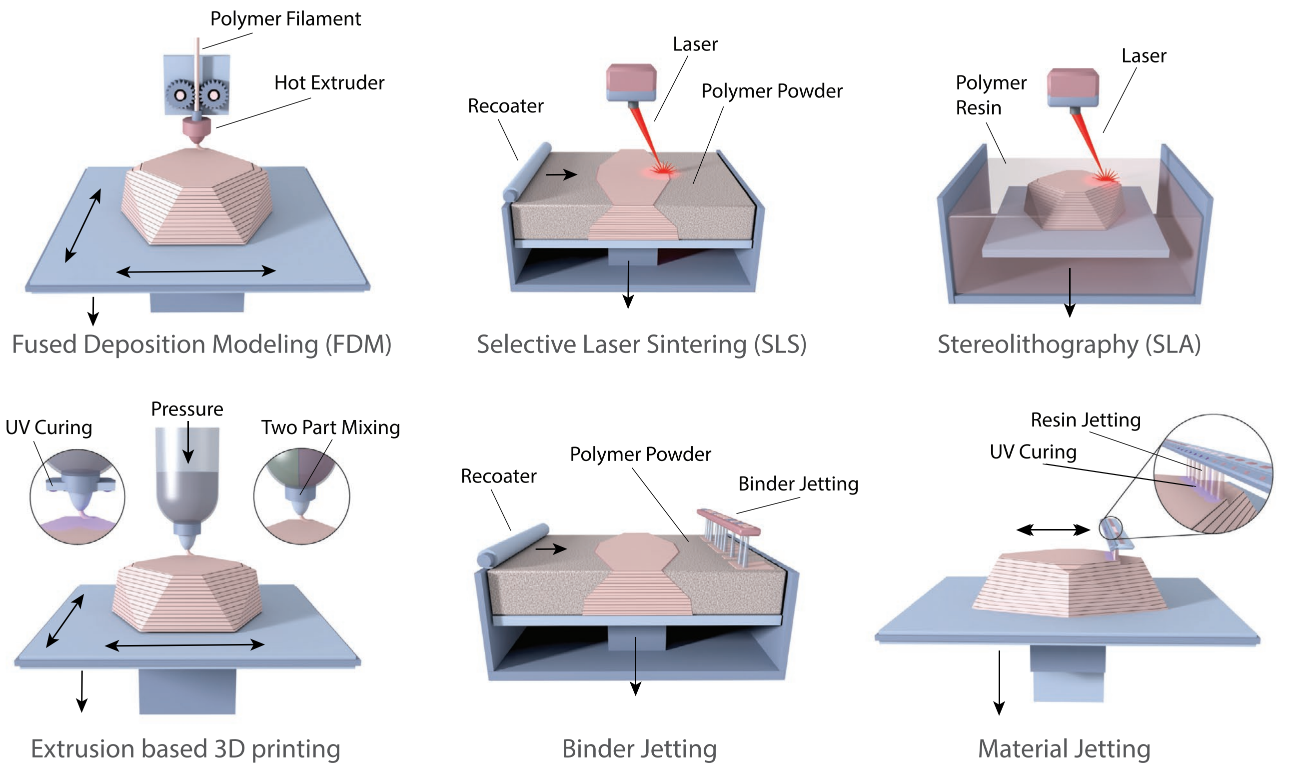

Figure 4. Schematics showing the most common polymer 3D printing technologies. All techniques build up the 3D object layer-by-layer. Fused deposition modeling (FDM) involves drawing a polymer filament through a heated extruder and onto the print bed which translates to produce a stack of object "slices." Selective laser sintering (SLS) involves coating a layer of fine polymer powder on the top of the build area. A laser is then used to selectively sinter the powder in the desired pattern following which a new layer of powder is deposited and the process repeats. Stereolithography (SLA) uses a UV laser (or a 2D light pattern) to selectively polymerize a layer of polymer resin in a vat. After a layer is polymerized, it is lowered into the vat and the new layer polymerized. This process repeats to build up the object. Extrusion based 3D printing involves forcing a liquid polymer through a nozzle where it can polymerize. The 3D object is built up layer-by-layer as with FDM. In some applications, UV lamps are added to photocure the polymer upon extrusion, and two-part mixing can also be performed using a mixing or coaxial nozzle. Binder jetting operates similar to SLS, however, a binder material is selectively extruded onto the top layer of powder instead of sintering via a laser. Material jetting uses 'ink-jet like print heads to selectively extrude polymer resin as the head passes over the build volume. The built layers are lowered and the process repeats to produce the 3D object, often with UV lamps to ensure curing. More advanced applications of this technique uses thousands of very small nozzles that can each extrude different materials to create multimaterial 3D objects, or in some cases, enable the mixing of materials during fabrication to produce customized material properties.

prosthetics fabrication are shown in **Figure 4**. Fused deposition modeling (FDM) feeds a solid polymer filament into a hot extruder nozzle. The nozzle melts the polymer onto the build plate as it is translated along the horizontal plane to build a solid layer.[102] The build plate is then moved downward (or the nozzle upward), to enable the fabrication of the next layer. FDM printers are one of the lease expensive, and some allow the use of multiple extruders in tandem to enable the fabrication of composite material objects.[103,104] They also have a broad range of low-cost materials available including both rigid and flexible polymers.[102] Extrusion-based approaches follow a similar process to FDM, in that the object layer is built up as the material is extruded, however, pressure is applied via either pneumatic or mechanical means to force out the liquid, resin, or gelatinous material.[105] Different adaptations of this approach, such as the addition of UV curing or multipart mixing, enables the use of photopolymers or two-part polymerization processes.[106] 3D material extrusion is also the basis for several direct 3D printing of silicone approaches.[107] Selective laser sintering (SLS) fabricates objects by depositing a thin layer of polymer powder across the build plate and then selectively fusing the polymer in the layer to produce the desired solid pattern.[108] The build plate is then lowered, a recoater deposits a new layer of powder over the previous layer and the whole process repeats. This continues until the object is formed. SLS is a rapid technique capable of very high resolutions and is compatible with a wide variety of polymers from rigid and strong to flexible materials.[109] Binder jetting is similar to SLS, however, instead of sintering the powder, a jet of a binder is extruded to form the solid material.[110] Many binder jetting printers use a large array of piezoelectric nozzles (similar to an inkjet printer) and can produce each layer rapidly (and some in full color by using a color binder on white powder material).[111] Stereolithography (SLA) is one of the oldest 3D printing technologies and uses a laser (or UV pattern projector) to selectively polymerize a photopolymer resin in a layer-by-layer manner.[112] This technology enables rapid printing of 3D objects with a very high degree of resolution and precision and includes the ability to use both solid and elastomeric photopolymers. Material jetting is similar to powder binder jetting in that an array of piezoelectric nozzles are used to selectively extrude a material, except that instead of a binder being deposited onto a powder, it is the polymer itself that is extruded.[113] Typically this material is a photopolymer, and a UV light is used to cure each layer as the nozzles pass over. After the desired layer is produced, the build plate is lowered and the process repeated. One advantage of this process is the ability to precisely control the deposition of the material and, with multiple micronozzles, enable the extrusion of different materials in the one pass of the print head.[21] This enables multimaterial objects to be built up and, in some cases, tens of thousands of nozzles can be used to extrude the raw polymers which are then combined prior to polymerization leading to tailorable material properties.[114,115]

4. Polymers in Prosthetics

Synthetic polymers are now widespread in contemporary prosthetics, having replaced many natural materials that were used prior to their introduction.[41] Their advantages include the ability to mimic native tissue both functionally and aesthetically, and provide superior safety, customizability and robustness. Traditional polymers, such as silicone and acrylic have been used in prosthetics for over 50 years[116,117] and their relevant characteristics are well established.[118] Newer and more complex polymers designed specifically for 3D printing have also recently entered the market.[18,42,49] In some of these cases, materials can be blended as desired during fabrication to produce biomimetic objects with functional gradients of mechanical properties.[119] Furthermore, traditional polymers are also able to be used in many 3D printed prostheses.[18] For example, the most common prosthetic material, silicone, is often cast in 3D printed molds for clinical use.[5,120] Research is also underway for direct 3D printing silicone via extrusion,[107,121] photocuring,[4,122] or material jetting methods,[15,123] although many challenges still remain.[124]

A modern soft-tissue prosthetic comprises a skin-like layer which is typically bonded to a substructure to maintain shape and, in some cases, include magnetic or mechanical attachment clips[125] (see Figure 2b). Traditional polymers used in the skin-like layers of prostheses include poly(vinyl chloride) (PVC), polyurethane elastomer, chlorinated polyethylene (CPE), and silicone.[126] New commercial blends of elastomeric materials optimized for 3D printing also have potential for similar use. Substructures and eye prostheses are typically constructed using rigid polymers, such as acrylic resins (such as PMMA) and rigid 3D printable polymers.[26] A significant challenge in multimaterial prostheses is bonding of the different materials, particularly in the case of silicones due to their difficulty adhering to other materials.[127,128] This issue can be alleviated with modern 3D printers that have multimaterial capabilities. The most advanced of these can selectively mix multiple materials for tailoring of the final material properties.[46] For example, a 3D object can be printed that smoothly transitions from rigid and transparent at one end, to flexible and opaque at the other.[21] The potential implications for prosthetics' fabrication are significant, allowing designs with personalized mechanical and visual properties based on the precise requirements of the patient.[42,129]

In the following discussion of the chemistry and properties of synthetic polymers for soft tissue prosthetics, the materials have been grouped into three sections; traditional polymers for prosthetics, silicone for both traditional and 3D printed prosthetics, and advanced polymers for 3D printed prosthetics. Traditional polymers are those with a long history of use in prosthetics and are applied to traditional fabrication approaches, such as molding and casting. Although silicone is also a well-established polymer for traditional fabrication approaches, its unique material properties make it highly attractive for use in 3D printing.[15] As such, there is much ongoing research in improving the 3D printing of silicone.[121,123] Additionally, some materials now used in 3D printing were developed well before 3D printing itself. However, in this report these materials are only discussed in the context of their application in 3D printing of soft tissue prosthetics. **Table 1** shows a summary of the materials discussed in this section, as well as their advantages and disadvantages in the context of soft tissue prosthetics, their fabrication approach, prosthetics applications, and a brief summary of their biocompatibility and regulatory status where available.

4.1. Traditional Polymers for Prosthetics

Despite the capabilities and promise of 3D printable materials, many polymers developed during the past century are still commonly used in the traditional hand-crafting and molding fabrication of personalized soft-tissue prostheses.[41] Their continued use is evident in the curriculums of educational institutions, where both traditional and advanced manufacturing techniques are taught. In Section 4.1, important properties and chemistries of a few of the key materials used in traditional hand-fabricated external soft-tissue prosthetics are summarized; plasticized PVC, polyurethane elastomer, CPE, and acrylic resin.

4.1.1. Plasticized Poly(vinyl chloride)

Plasticized PVC was a broadly used soft tissue prosthetic material and is still in use today for gloves for prosthetic hands.[130] Due to its lower costs and greater tear strength and lower weight, it was once preferred over silicone.[131,132] The 1970s, however, saw its use dwindle in place of newer room-temperature vulcanizing (RTV) silicones with improved tear strength.[38] Compared to PVC, RTV silicone prostheses are easier to fabricate with superior skin-like properties and color integrity.[38] A variant, PVC plastisol resin, can be placed into high-temperature molds which are heated to 200 °C to initiate polymerization.[133,134] Plasticizers enabling skin-like properties can leach, however, with important biocompatibility implications, such as carcinogenicity, reduction of birth weight for exposed fetuses, shortening of the male anogenital distance, reduction of levels of serum testosterone and spermatocyte numbers, and disruption of the reticulo-endocrine systems.[135–137] In addition to its toxicity, PVC plastisols possess relatively low tear resistance and are also environmentally unstable with susceptibility to drying, cracking, tackiness, and color changes.[138,139] Although PVC can be reinforced to improve its materials properties, it has limited use in modern prosthetics.[140]

Table 1. Comparison between various materials used in soft tissue prosthetics.

	Polymer	Description	Advantages	Disadvantages	Prosthetic fabrication/processing	Prosthetic application	Biocompatability/regulatory status
Traditional polymers	Plasticizedpolyvinyl chloride	Soft tissue-like material, limited use in modern prosthetics.	Lower costs, higher tear strength, lighter weight compared to silicone[131]	Plasticizers leach, causing biocompatibility problems[136]	High-temperature molds and heat polymerized	Gloves for prosthetic hands. Soft tissue prosthetic material.	Medical grade (FDA) available for glove applications.[318]
	Polyurethane elastomer (thermoset)	Tailorable physical and chemical properties throughout material[141]	Designable flexibility, elasticity, softness, hydrophobicity,[144] environmentally stable, high tensile and tear resistance[143]	Sensitive to reaction details and difficult to work with.[143] Moisture during processing changes properties.[145]	Can be molded at 100 °C.	Bulk elastic polymer, as prosthetic liners, and foam references	Medical application of PE widespread with thousands of devices FDA approved. Biocompatable[319]
	CPE	Similar properties to silicone but thermoplastic and lower cost.	Lower cost than silicone and made to be a thermoplastic. Easier to repair, reline, and be reconditioned.[41]	Use in prosthetics is limited possibly due to perceptions that fabrication is more complex than silicone during fabrication.[41]	Added to a mold and either heated to 110–115°[150] or alternatively in a pressure cooker.[148]	Extraoral maxillofacial prostheses as alternative to silicone.[41]	Less irritating to mucosa, less toxic than thermosetting silicone, noncarcinogenic.[41,320]
	Acrylic resin	PMMA. Clear rigid, mostly used as dental base material, orbital prostheses and prosthetic substructures.	Ease of manipulation with doughy consistency of mixed material, minimization of the heat produced and autopolymerization.[153]	Formation of pores (or voids), volumetric shrinkage, incomplete polymerization, and tendency to fracture[154] introducing toxic chemical residues[159]	Moldable and hand formable two-component system and doughy consistency of mixed material.	Orbital prostheses, reinforcing material, or prosthesis substructure.	Biocompatible for implantation. Used widely in orbital prosthesis, dental applications and as bone cement.[321]
Traditional and 3D silicone	Silicone	PDMS is the most widely used facial prosthetic material.[41]	Skin-like flexibility, heat resistance, biocompatibility and intrinsic transparency.[41,169,170] Easy to work, mold and is 3D printable.[173]	Higher costs. RTV-2–selective adhesion, hydrophobicity, difficulty extrinsic staining, short working time and impurities reducing curing efficiency.[172]	Molds using RTV addition polymerization most common method.[41] Ongoing research into 3D printing.[322]	Extraoral maxillofacial prostheses, e.g., face, nose, ear, hand, breast.	Biocompatible medical grade silicone widely used in healthcare for decades.[323]
3D printable materials	3D printable elastomeric material	Thermoplastic elastomers/polyurethanes, elastic resins, polyester elastomers, photopolymers, proprietary blends,	Faster and more accurate prosthesis fabrication than conventional production.	Biocompatibility remains to be evaluated for many materials. Printing impact material properties[202]	3D printable using several different approaches (please see Figure 4)	Soft tissue components of Extraoral maxillofacial prostheses.	Only limited number of certified 3D printable elastomerics are certified biocompatible.[51,52,114,202]
	3D printable rigid materials	Acrylonitrile Butadiene Styrene, PLA, Nylon, Polyether ether ketone.	3D printing with digital design tools, accurate and more sophisticated. Potential multimaterial composite prosthetics.	Lower-cost 3D printing may impact final part stability. More capable 3D printers with biocompatible materials relatively high cost.	3D printable using several different approaches (please see Figure 4)	Support structures and rigid framework for complex/composite prostheses.	Several certified biocompatible 3D printable rigid polymers available[51,52]
	Multimaterial polymer jetting	Uses inkjet (piezoelectric) or similar technology to selectively deposit liquid material.	High layer resolution of 0.1 mm as well as the ability to produce complex multimaterial object with variable mechanical properties.[217]	Many elastomeric materials have lower durability compared to silicone. Very high cost of 3D printers.	3D printable (please see Figure 4)	Complex multimaterials with tailorable mechanical properties.[129]	Some materials certified biocompatible,[52] mixing biocompatible and nonbiocompatible materials possible.

4.1.2. Polyurethane Elastomer (Thermoset)

Polyurethanes (PU) were discovered in 1937 by Otto Bayer and are still in use in prosthetics as elastic polymers, liners of prostheses, and reference models.[141,142] A particularly useful property of polyurethanes is the ability to tailor their physical and chemical properties throughout the material by varying the reactions of isocyanates and polyols during synthesis.[140,141,143] For example, a soft skin-like feeling can be produced by including more polyols, such as aliphatic diols, polyesters, or hydroxyl terminated polyethers. The longer chain molecules form the soft segments and add elasticity, flexibility, softness, and hydrolytic degradation resistance.[144] Prosthetic service life can also be improved by adding hard polymer chain segments using the isocyanate groups which can be either di- or polyfunctional.[133,140] For example, improved resistance to UV damage and hydrolysis can be achieved using aliphatic groups, whereas improved mechanical properties results from the addition of aromatic groups.[144]

Crosslinking of PU can also be achieved at 100 °C, lowering the cost of molds for the fabrication of prostheses or components compared to higher-temperature crosslinking.[133] Typically, the first stage requires the preparation of diisocyanate-terminated prepolymers, which are then joined by adding the highly reactive diol chain extender/crosslinkers.[141,143] The chain sequence of hard and soft segments can be controlled through this reaction. This synthesis, however, is stoichiometric and therefore very sensitive to the details of the reaction, making this polymer difficult to work with.[143] This process is also very sensitive to moisture which may lead to changes in the prosthesis' visual and tactile properties, as well as reducing isocyanate group reactivity and subsequent incomplete polymerization.[145] This may irritate the skin of the wearer due to the resulting polyureas.[140,145] For prosthetics, PU can be colored intrinsically and extrinsically, is environmentally stable, has excellent tear resistance and a high tensile strength and does not require the addition of plasticizers for a low modulus of elasticity.[140,143]

4.1.3. Chlorinated Polyethylene

At the National Institute of Dental Research Conference in 1973, it was proposed to investigate various industrial rubbers as potential prosthetic materials.[146] Three years later, a grant was used to fund research which led to the formulation of thermoplastic CPE, a new prosthetic material. CPE can be processed to have similar properties to silicones, but lower cost and a thermoplastic.[147] For prosthetics, this makes it easier to repair, reline, and be reconditioned and reprocessed for small corrections.[139,147] It also has a greater tear strength and surface wettability than silicone, can be used with many adhesives, low toxicity, is noncarcinogenic, does not support fungus growth and is less irritating to the mucosa than silicone.[139,148] Patient experience is also supportive. A clinical trial comparing silicone and CPE facial prostheses found those with previous experience of silicone prosthesis preferred silicone, and those with no previous experience expressed no preference.[147]

CPE is produced through the random chlorination of the polymer chain of high-density polyethylene in an aqueous slurry.[149] It is then processing into large sheets on heated mills. The processed CPE is added to a prosthesis mold and either heated to 110°–115°[150] or alternatively placed in a pressure cooker for 10 min.[147,148] Following this initial process, more CPE is added and heated repeatedly until the mold is filled.[147] Although CPE has comparable properties to silicone and is also a thermoplastic, its use in prosthetics is limited. This may be due to perceptions by prosthetic technicians that CPE fabrication is more complex, has more flaws, and has a higher likelihood of failure during fabrication compared to silicone.[147]

4.1.4. Acrylic Resin

Acrylic resin, or polymer PMMA, was developed in 1944 due to a shortage of glass.[36] It is a rigid clear polymer with applications in dentistry and orbital prostheses fabrication and substructures for materials, such as silicone.[140,151,152] It comprises methyl methacrylate (MMA) units[152] which include a two carbon atom backbone.[152,153] A method developed in 1936 improves the fabrication of acrylic resin to speed up curing. This approach is still used today in dentistry and prosthetics.[152,154,155] The major advantage of this approach is improved manipulation because of heat minimization, doughy consistency, and minimization of volumetric shrinkage.[152] Autopolymerization can also be achieved by adding chemical agents to start polymerization.[156]

Although highly suited for use as orbital prostheses, as a reinforcing material, or as a prosthesis substructure,[157] material limitations include shrinkage of material, pore formation and fracture tendency.[154] Another challenge during fabrication is the introduction of pores which leads to incomplete polymerization.[152] This adversely affects mechanical properties, such as strength, surface roughness, and hardness[152,158,159] and introduces toxic chemical residues.[151,158] Pores also act as sites for stress concentration[152] and can enable microbial growth, altering the material and potentially infecting the patient.[159] Another significant issues are residues of toxic chemical which may occur due to incomplete polymerization.[151,158] For prosthetic reinforcement applications, acrylic resin can be strengthened.[154,160–168]

4.2. Silicone for Traditional and 3D Printed Prosthetics

Silicone, or poly(dimethylsiloxane) (PDMS), is the most widely used facial prosthetic material due to its skin-like flexibility, heat resistance, biocompatibility, and intrinsic transparency.[41,169,170] It owes its unique properties to its inorganic siloxane structure which has structural similarities to the carbon backbone of organic polymers.[171,172] Crosslinking can occur in silicone via condensation polymerization, free radical polymerization, and addition polymerization.[173,174] They can be further divided into RTV or high-temperature vulcanizing (HTV) (**Figure 5**). Although many fabrication methods have been attempted over the years, room temperature addition polymerization is the most common approach.[41] Several methods for 3D printing of silicone have also been recently developed including SLA

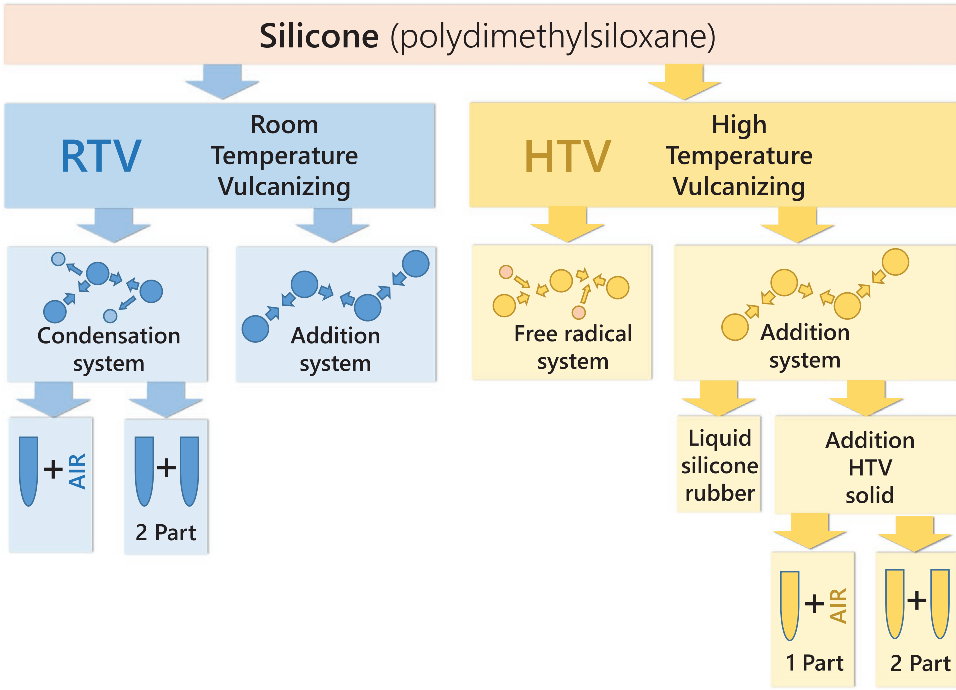

Figure 5. Outline of the various polymerization approaches for silicones. The two fundamental approaches are described as either RTV and HTV.

techniques (vat polymerization), material jetting, and material extrusion, with crosslinking occurring via addition polymerization or UV curing.[175]

4.2.1. Room-Temperature Vulcanizing

Crosslinking of RTV silicone occurs using either addition or condensation polymerization via a crosslinking agent and a catalyst. The advantage of RTV crosslinking is that a mold can be made from low-cost plaster and dental stone (gypsum) for silicone casting and curing.[140] Whereas condensation polymerization systems can be either one-part (RTV-1) or two-part (RTV-2), additional polymerization systems are only RTV-2.[176]

When used with a crosslinker and organotin catalyst (e.g., methyl triacetoxy silane), condensation polymerization can occur at room temperature.[76,172,174] This process begins with hydrolyzation of the functional groups, creating silanols that initiate condensation and a reaction by-product.[172,174] This is commonly achieved via functional groups, such as alkyloxy and acetoxy groups which release methyl alcohol and acetic acid, respectively.[171,172]

RTV-1 condensation systems are found in adhesives and sealants.[176] On exposure to atmospheric moisture, crosslinking immediately begins.[174] Consequently, they must be kept in sealed containers. One of the limitations for their use in prosthetics is the difficulty producing parts with thicker cross-sections as moisture cannot penetrate deep enough for polymerization.[171] These systems do, however, find use in prosthetics, such as in medical adhesives and external colorants for prostheses applications.[177] They also suffer from other limitations, such as their relatively long polymerization time and the production of acetic acid which is a skin irritant.[177]

RTV-2 condensation polymerization systems begin crosslinking when a curing agent and base combine.[171,172,174,176] Silastic 382 (Dow Corning Company) is an example of commonly used prosthetic materials of this type which was once common in implants and maxillofacial prostheses until the 1980s where they were discontinued due to safety concerns.[140,178–181]

RTV-2 addition polymerization systems are often known as RTV platinum catalyzed silicones, and form when silyl hydride groups and unsaturated vinyl siloxanes react when triggered by a platinum catalyst and begin to polymerize.[174] These RTV silicones can also be heat cured in order to reduce curing time.[174] With this polymerization approach, shrinking is reduced due to the lack of by-product in this reaction.[172] For prosthetics, some disadvantages of this type of polymerization includes selective adhesion, hydrophobicity, difficulty with extrinsic staining, short working time, and impurities reducing curing efficiency (e.g., amines, sulfurous, or other catalyst poisons).[172] RTV platinum catalyzed silicones are highly popular with prosthetists and are among the most used material in maxillofacial prosthetics.[41]

4.2.2. High-Temperature Vulcanizing

HTV crosslinking occurs via addition or free radical polymerization.[172] The high temperatures involved in crosslinking HTV silicones between 100 and 200 °C for increased working times than RTV silicones of up to 30 min. Additional polymerization HTV silicones are generally transparent with no yellowing, odorless, can be demolded easily, do not require any processing after curing and have relatively high tensile and tear strength.[76,176] Furthermore, altering the amounts of each of the two components changes the final silicone's flexibility. An example of a two-part addition curing compound is liquid silicone rubbers, which can be produced with a consistency from low to high viscosity,[172,176] and has an tailorable curing rate which is relatively slow at room temperature and more rapid at higher temperatures.[172,176] Free radical HTV silicones (peroxide-initiated reaction systems) have use in producing silicones with a high-consistency, high tear resistance, and are thermally stable.[140,171,172] However, they suffer from yellowing after curing, have a strong odor both during and after production, and are tacky to touch with high surface friction. They also can involve peroxide residues that create voids in the cured silicone and can lead to depolymerization at higher temperatures.[171,174,176]

Silicone's mechanical properties are influenced by molecular weight, crosslinking efficiency, and the addition of any fillers or pigments.[76,170,182] For example, the strength and flexibility of the polymer is directly affected by molecular weight distribution.[76,182] Silicones can also be strengthened using a filler, often referred to as extending.[176] This is due to a dissipation of energy during deformation of the material so molecular chains can slide past each other more easily.[183,184] The most common silicone filler is hydrophobic surface treated silica can increase strength, hydrophobicity, loss and storage modulus, and damping factor, as well as decrease elasticity.[171,176,183] Titanium, zinc, and cerium nano-oxides have also been examined for use as fillers.[185]

In many applications, the silicone prosthesis needs to be bonded to a substructure, and in some cases to an osseointegrated posts for use with clip or magnetic anchoring.[125] Direct chemical bonding between acrylic and silicone difficult, due to their different chemical structures inhibiting molecular adhesion.[37,186] Adhesives have also been found to be insufficient, however, primers containing both an adhesive agent and solvent have been found the enhance bond strength.[37,187] Mechanical interlocking of surface roughness and design methods for retaining the silicone surface with substrate surface features can also be used to improve silicone adhesion. In many cases following fabrication of the prosthetic, extrinsic color is painted to add fine detail and improve realism.[188] Matching the patient's skin color is extremely challenge and several techniques have been developed to measure and determine the correct pigmenting for each patient, such as spectrophotometry and colorimetry with color formulation algorithms to determine accurate pigmenting.[189,190]

4.2.3. Silicone for 3D Printing

As the most commonly used soft-tissue prosthetic material, it is no surprise that there are several ongoing efforts to 3D print silicone.[123] Current approaches can be broadly classified as either indirect or direct.[191] Indirect approaches typically use low-cost 3D extrusion printers to fabricate rigid polymer molds for curing silicone.[192] The use of a mold means that polymerization occurs uniformly throughout the bulk of the silicone producing a result similar to traditional approaches. Direct approaches, on the other hand, involves the layer-by-layer extrusion, jetting, or polymerization of silicone.[107] Although desirable for ease-of-fabrication, the use of direct 3D silicone printing in prosthetics is limited due to visible layering from the progressive polymerization, potentially rendering the printed prosthetic visually unappealing.[4,15,17,107]

One extrusion approach utilizes a two-part RTV silicone tailored to achieve optimal mechanical characteristics.[18] In this method, the two components are separately loaded into syringe pumps and extrude the components into a mixing extruder prior to deposition onto the build plate. To reduce the curing rate and extend the working time, a moderator can be incorporated.[17] The viscosity of the printed silicone can also be increased by adding a thixotropic for a more stable and rigid 3D printed structure.[17] Alternative approaches to 3D print silicone include extruding an RTV moisture-cured silicone elastomer in place of a two-part mixture,[193] or using a photoinitiated curable silicone which is then cross-linked using a UV lamp.[107] Extruding silicone through nozzles is performed using either pneumatic or mechanical methods. Consequently, theoretical modeling of viscosity through various nozzle designs is of critical importance.[16,194] Another direct silicone 3D printing approach, the Drop-on-Demand system (Wacker Chemie AG, Germany), selectively deposits material droplets onto a build area, which are then cured using a UV lamp.[4] Silicone prostheses fabricated using this method demonstrated an acceptable clinical fit due to the precision of the digital processing pipeline, however, the layer thickness of 0.4 mm preventing the achievement of the thin margins of traditionally produced nasal prosthetics which is important for blending with skin.[4]

Vat photo-polymerization is yet another direct silicone 3D printing approach under development.[107] Similar to SLA this method was first introduced in 2014 to print PDMS microfluidic membranes. It relies on the use of a digital light processing system to selectively photocure a layer of resin polymer.[195,196] 3D objects are then built up by depositing successive resin layers for photocuring. A recent support-free method was introduced that uses hydrostatic forces inside the resin vat to maintain structure in soft polymers during fabrication, allowing for the fabrication of complex objects with overhangs.[197,198] Key to this approach is the use of a low one-photon polymerization process to initiate polymerization just under the resin surface. More recently, a patent describing a similar approach was granted to Dow Corning for a 3D printing method using a photocurable silicone.[15] The patent also describes a method for partially curing of the layers so adjacent layers not only physically bond, but also chemically bond on subsequent layer curing.[15]

4.3. Advanced Polymers for 3D Printing

Developments in advanced manufacturing are driving innovation in the design, production, and materials of prosthetics. As summarized in Section 3 and Figure 4, the various approaches to 3D printing can impact the properties of the final object produced.[175] Although most techniques can print with elastomeric and solid materials, the fundamentals behind each approach lends itself to a variety of advantages and disadvantages. Many of the material properties discussed in Section 2 and Figure 2a are influenced not only by the material, but also the 3D printing approach. Additionally, the layer-by-layer fabrication of 3D printed objects results in different mechanical characteristics compared to traditionally cast objects, often with an anisotropic variation in final mechanical properties.[199] For 3D printable elastomeric (soft) materials, most techniques use the polymer in one of three forms; photocurable resins, thermoplastic monofilaments, and polymer powders (see Figure 4), usually comprising some form of photopolymers, thermoplastic urethanes or other thermoplastic elastomers.[175] Although of limited application in the direct fabrication of soft tissue prostheses, 3D printable rigid materials are often used in the production of 3D printed molds in place of hand-crafted molds (see **Table 2**).[200] They also have potential in the fabrication of rigid frameworks to support complex prostheses, or for ocular prosthetics.[201] One of the most promising approaches for fabricating complex multimaterial and composite prostheses is polymer jetting which can produce objects with a variety of colors and material properties in a single print.[113]

4.3.1. 3D Printable Elastomeric Materials

Many modern commercial 3D printers have multimaterial capabilities, including metals, ceramics, and polymers.[48] Although the particular elastomeric polymers and blends used in 3D printing vary from manufacturer to manufacturer, they are generally some form of photopolymers, thermoplastic urethanes or other thermoplastic elastomers (such as ester based thermoplastic polyurethane (TPUs), polyether block amides or Styrene-butadiene copolymer).[202] Many printer and material suppliers also offer biocompatible certified materials, many of these are only available in rigid or rubber-like properties.[51,52] The advantages of 3D printable elastomeric materials over some of the more traditional materials, or even 3D printable silicone, can often revolve around their ability to be 3D printed rather than the material itself.[203] One of the common elastomeric materials used in the production of hand prosthetics is TPU.[204] TPUs are block copolymers with alternating hard and soft segments which can be manipulated to produce a range of hardness of

Table 2. Brief summary of six recent publications using 3D printing for each of the soft tissue prosthetics; ear, nose, face, eye, and hand.

	Publication	Description	3D printing
Ear	McHutchion et al. 2020	Prosthetic ear molds FDM 3D printed using ABS and filled with silicone	FDM ABS mold
	Thomas and Singh 2020	3D printing patient specific cosmetic prosthetics-silicone printing	Silicone 3D printing
	Artioli et al. 2019	3D printed FDM mold for silicone ear prostheses	FDM PLA mold
	Unsal et al. 2019	CT scan of patient, 3D printed FDM model, then traditional prosthetic	FDM work model
	Arias et al. 2019	Structured light scan of patient, 3D printed FDM mold filled silicone	FDM ABS mold
	Unkovskiy et al. 2019	Ears of 23 subjects scanned and 3D printed to validate digital workflow	FDM, SLS, SLA
Nose	Chen et al. 2020	3D printed custom bandage following rhinectomy using medical grade polymer	Multijet resin
	Somohano Marquez 2019	CAD design and 3D printed working model of nose to help traditional fabrication	SLA work model
	McHutchion et al. 2019	3D printed nasal prototype and substructure using elastic and solid materials	Multijet work model
	Shikara et al. 2018	3D printed molds for silicone prostheses from high-impact polystyrene (HIPS)	FDM HIPS model
	Nuseir et al. 2018	3D print flexible prosthetic nose – TangoPlus (Stratasys Ltd) not biocompatible	Multijet elastomer
	Abdullah et al. 2018	3D print mold of patient's nose and filled with silicone and hand post process	FDM mold
Face	Lin and Yarholar 2020	Used 3D printing approaches to assess craniofacial models, splints, and implants	Assessed various
	Cevik and Kocacikli 2020	Case study, 24 year old man silicone 3D printed maxillofacial prosthesis	Silicone 3D printing
	Jain et al. 2019	Hi resolution 3D print facial surface template using different blends of materials	Multijet multimaterial
	Unkovskiy et al. 2018	Drop-on-demand direct 3D printing of silicone facial prosthesis	Silicone 3D printing
	Bockey et al. 2018	3D print 32 face and prosthetics models to assess suitability of approach	Multijet multimaterial
	Jamayet B et al. 2017	Case study of 3D printed face prosthetic, FDM mold to make silicone prosthetic	FDM mold
Eye	Kim et al. 2019	Orbital & ocular prosthesis 3D printed mold using SLA printer for silicone molding	SLA biocomp. resin
	Beiruti et al. 2019	3D-Printing custom ocular prostheses using various 3D printing technologies	Assessed various
	Jain et al. 2019	3D printed working model of conformer (fits into skull to attached prosthesis)	FDM PLA model
	Liu et al. 2018	Fabricated a two piece negative mold of orbital prosthesis for silicone fabrication	SLS Polymide
	Ko et al. 2019	SLA printed ocular prosthesis with biocompatible photopolymer resin as base	SLA photopolymer
	Alam et al. 2017	3D printing of two ocular prostheses with biocompatible PMMA and hand painted	PolyJet PMMA
Hand	Alturkistani et al. 2020	3D printed palm and fingers of partial hand prosthesis using multimaterials	FDM PLA & TPU
	Eshraghi et al. 2020	Prosthetic printed in thermoplastic elastomers (TPU), PVB outer for biocompatability	FDM TPE
	Yabuki et al. 2019	Bone parts of prosthetic hand 3D printed for testing cosmetic outer materials	FDM ABS
	Young et al. 2019	Case study of personalized 3D printed partial finger prosthetic	FDM PLA
	Lee et al. 2018	3D printed prosthetic hand made from nontoxic flexible thermoplastic elastomer	FDM TPE
	Radosh et al. 2017	Hand and arm prosthesis printed with dual material printer, rigid core and soft outer	FDM ABS & TPU

the material. The materials flexibility is due to both of these hard and soft segments as well as its chemical structure. The hard segments are generally isocyanates (either aliphatic or aromatic), and the soft segments are a reacted polyol.[205] TPUs are commonly used in low-cost FDM printing and are available in filament rolls as well as in SLS, SLA printing techniques,[48] with many relevant material properties, such as flexibility, durability, and is available as a medical grade polymer.[206]

Many commercial 3D printer manufacturers supply a large range of elastomeric polymers for their 3D printing technologies. Often these materials are proprietary and designed only for use in the certified printer. For example, 3D systems (South Carolina, USA) currently have nine proprietary elastomeric materials available for their SLS, SLA, and material jetting 3D printers[109] as well as their noncontact membrane digital light printing technology.[207] These include TPUs as well as monofunctional aliphatic urethane acrylate blends and other proprietary polymers. Flexible materials are also available for fused deposition modeling printers from Stratasys (Minnesota, USA) and other 3D printer suppliers, including many that are biocompatible.[208] Stratasys supply advanced thermoplastic elastomer (TPE) blends for their FDM printers as well as a range of rubber-like photopolymers, such as their Tango range for their polymer jetting printers.[209]

An example of a two-step approach to 3D printing a prosthetic with elastic properties involves first binder jetting on a starch powder, and then infiltrating medical grade silicone into the starch model.[54,210,211] The inclusion of silicone improves elasticity; however, the resulting material has lower elongation and lower tensile strength, and is significantly harder compared to pure silicone.

4.3.2. 3D Printable Rigid Materials

3D printable rigid materials have applications in modern prosthetics fabrication processes for either production of the molds which are then used in flexible polymer casting, or potential for 3D printing rigid support structures for composite material prostheses.[212–214] The relative infancy of 3D printable elastomers in prosthetics means that nearly all recent publications that involve soft-tissue prosthetic 3D printing used some form of rigid polymer for producing molds (see Table 2). The following is a brief discussion of some of the most commonly used 3D printable rigid materials that are not directly used in the prosthetic itself.

ABS is a strong, durable, and chemically resistant polymer with a low melting temperature making it ideal for use in FDM printing.[88,212,214,215] Another widely used FDM material for producing prosthetics molds is poly(lactic acid) (PLA) which is a popular polymer with the monomer made from fermented plant starch and is available as a low-cost filament roll.[213,216] Many proprietary rigid materials are also available from commercial 3D printer manufacturers, with polypropylene-like materials, ABS-like materials, nylon materials, and proprietary blends.[52,217] These are suitable for a wide range of 3D printing platforms and are available as powders (for SLS and binder jetting) and resins (for SLA and material jetting).[52]

In addition to 3D printing of molds, some rigid 3D printable materials have been used in the production of prosthetics models, ocular prostheses, and the rigid frameworks within prosthetics hands.[201,218] For example, polymer jetting rigid materials have recently been used to produce 3D models of the prosthesis to augment the traditional wax modeling and prosthesis fabrication process.[28,216,219] This allows digital design of the prosthesis using CAD software based on 3D patient data to improve the accuracy of the prosthetic. Another polymer, Polyamide (Nylon), has recently been used as the rigid 3D printing material to fabricate a two piece negative mold for an orbital prosthesis[220] and a special biocompatible 3D printable PMMA resin was 3D printed using a material jetting approach to directly print personalized ocular prosthetics which were subsequently hand painted.[221]

4.3.3. Multimaterial Polymer Jetting

This 3D printing technique uses inkjet technology to deposit liquid material selectively, layer-by-layer.[222] The material is then crosslinked using a UV lamp for photocurable polymers, or via cooling for thermoset materials (e.g., wax). The process is repeated for subsequent layers to build up the 3D object. Some of the advantages of material jetting over other methods include a high layer resolution as well as the ability to produce complex multimaterial objects.[223] Polymer jetting printers like the ProJet series from 3D Systems (South Carolina, USA) or the ProJet series from Stratasys (Minnesota, USA) are capable of combining multiple materials on-the-fly during printing. In effect, these technologies enable personalization of not only shape and color, but also the mechanical properties of the material. For example, the ProJet 5500X is a recent printer from 3D Systems that can combine up to two photocurable polymers at the same time, including combinations of rigid and flexible photopolymers from their large range of base materials.[222]

In the context of prosthetics, a polymer jetting 3D printer was recently used to produce a composite prosthetic nose and ear,[56,224] combining "Tango Plus," a transparent rubber-like material[209] with "Vero," a rigid opaque material.[225] While "Tango Plus" provides a soft feel which is ideal for prosthetic materials, it was found to be colorless. To overcome this, the "Vero" material was used for coloring and to provide rigidity for mimicking cartilage. Although the printer used for these prosthetics could use 3 materials simultaneously, its ability to produce accurate coloring was limited. Another limitation was rupturing of the flexible material during support material removal in thin regions.[56,224] Other applications include hollow prosthetic eyes fabricated using polymer jetting technology and hand-painted to match the patient.[221] This approach was found to be superior to traditional methods, with significantly reduced fabrication time and improved patient comfort.[56,224]

4.4. Focus on Degradation

Both chemical and mechanical changes limit the service life of all prostheses. Additionally, they are often exposed to mechanical stresses, ultraviolet radiation, water, acidic perspiration, alkaline perspiration, sebum, biological contamination, disinfectants and soaps, extreme temperatures, adhesives, chemical interactions, crack formation, and general chemical degradation.[71] These factors combine to reduce the natural look and feel of a prosthetic, which is undesirable given the costs and complexities of fabrication.[89]

4.4.1. Chemical Degradation

Chemical processes can continue within polymers long after crosslinking has occurred which negatively impacts their mechanical properties.[226,227] For example, PVC is subject to enhanced degradation from unsaturated bonds, open chain end groups, and branch points. This leads to color changes and loss of mechanical properties.[228] CPE degrades over time via chain scission reactions which promotes polymer softening. Silicone, on the other hand, undergoes hardening due to continued crosslinking and increases in elastic modulus, glass transition temperature, and viscoelasticity.[229] Maximum stress and strain also decreases, as well as a reduction in tear strength.[71,72,229] Age related degradation of acrylic resins in prosthetics leads to unwanted color changes and a greater tendency to deform or fraction.[230] This is exacerbated by mechanical loading during normal use with material fatigue and crack propagation initiating.[231] Internal and surface stresses within acrylic can also form due to thermal expansion differences between the resin and other attached materials.[231]

4.4.2. Ultraviolet Radiation and Weathering

Exposure to sunlight, rain, wind, and aerosol pollutants also degrade the chemistry of many polymers over time, particularly for the exposed skin-like components of prostheses.[232] For example, environmental degradation of silicone is predominantly due to photo-oxidation from ultraviolet radiation.[187] This degradation mechanism involves the formation free radicals followed by propagation and finally termination when chain crosslinks are created by the inter-reacting radicals.[233] Another skin-like prosthetic polymer, CPE, also degrades due to UV exposure exhibiting an increase in maximum stress and strain, and a reduction in yield stress and strain, compression and tensile elastic modulus, and hardness.[233]

4.4.3. Skin Secretions

Perspiration and skin secretions also adversely affect material properties.[67,234] Studies of different commercial silicones immersed in simulated skin secretions found that the absorption of perspiration weakens the silicone and thereby increases its hardness and elasticity at the same time.[234] Sebum was found to interact with the surface of the silicone showing results varying widely depending on the silicone type. CPE prosthetics also degraded when placed in simulated perspiration solution to mimic 1.5 years of use, with increased elasticity, hardness, glass transition temperature, increased viscoelastic parameter, higher melting temperature, and color degradation all apparent.[235] Overall maximum stress and strain, however, were not observed to significantly change.[235]

4.4.4. Microbiological Degradation

Skin contact also can produce microbial growth which adversely affects both mechanical properties and prosthesis appearance, potentially causing skin irritation and infection.[83] The growth of microorganisms is generally not supported by silicone itself, however, surface roughness and porosity can enable colonization by commensal microorganisms that can form biofilms.[83] Surface roughness on molds can also be transferred exacerbating this problem.[83] Although regular cleaning and disinfecting can extend the life of a prosthesis, cleaning products, and disinfectants also degrade silicone.[236] The effect of different disinfection methods, such as sodium hypochlorite solution, microwaves, commercial disinfectants, chlorhexidine gluconate, soaps, and effervescent tablets have all been investigated.[237] Neutral soap increases material hardness and elastic modulus in silicone.[238] Storage in commercial disinfectant also leads to increased material harness and a reduction in tear strength.[237] The impact of microwaving is less clear, however, with hardness only slightly decreasing,[236] but increasing during microindentation tests.[238] Cleaning also affects acrylic resins due to their tendency to absorb water in a process known as imbibition.[231] Recently, a method to include bactericidal properties was studied by including poly(diallyldimethylammonium chloride) into silicone.[239] Similarly, the effect of surface roughness on biofilm development, including the addition of a photopolymerized glaze, was investigated for ocular acrylic resin prostheses.[240]

4.4.5. Color Change

One of the most visible effects of prosthetic degradation involves color changes.[68] For silicon prosthetics, both pigmented and unpigmented silicones undergo color change, however, the change is more rapid where pigments have been used.[72,241] In addition, organic pigments in silicone are more susceptible to color change than inorganic pigments.[230,242] Further complicating matters, the rate of color change depends on many factors including the pigment type, manufacturer, and original color.[243,244] Consequently, discoloration may occur at different rates for different prostheses on different individuals. Color stability can be promoted in silicones through the use of additives such as barium sulfate (0.2 wt%),[245] titanium dioxide nanoparticles,[150] and commonly used opacifiers.[246] Opacifiers, however, tend to increase degradation of the mechanical properties.[246] Other factors, such as skin secretions also increase the rate of color change for silicone prostheses.[67,234,247]

4.4.6. Lining

To overcome some of the materials' shortcomings of using silicones in prostheses, polyurethanes can be used as liners.[248] This improves tear resistance in the thin regions of prostheses and allows water-based adhesives to be used. The liners also seal the silicone from oils, and increases the smoothness of the surface contacting the patient, thereby improving comfort and ease of cleaning.[249–252] Despite these advantages, the lining process itself is potentially lengthy and sophisticated,[249] and polyurethane has a greater vulnerability to biofilm formation compared to silicone.[253] This is largely due to the appearance of microcracks on the material surface when immersed in water.[254]

5. Clinical Applications

Tissue loss or disfigurement negatively impacts body-image leading to psychological, social, and financial disadvantage.[255] This is particularly the case for young children who are undergoing personal and social development and may have a congenital condition affecting their development. For children, poor self-body image is compounded by teasing which, for microtia (malformation of the outer ear), begins between the ages of 2–5 years old and correlates with feeling sad, worried, and mad about their condition.[256] Ear reconstruction decreases teasing and negative emotions in all ages.[256] With microtia (undeveloped ear), psychosocial difficulties begin at around 8 years old, but improve significantly following surgical correction. Unsuccessful or poor surgical correction, however, negatively impacts body image. These results have also been shown in the case of cleft lip, with 62–75% of affected children suffering teasing.[257,258] Similarly, body image and mental health can suffer in tumor surgeries, such as mastectomy.[259–261] Although reconstructive surgery is available for many conditions, the relatively high costs and often negative patient experience means that for many people, nonpermanent prosthetic treatment is preferred.[262] Newer and upcoming surgical approaches, such as biofabrication and tissue engineering (the application of 3D printing processes to regenerative medicine) promise improvements over traditional corrective surgery.[263] These, however, are still largely in the early development stage with very few clinical studies demonstrating their efficacy. Although many soft tissue prostheses are still created using traditional hand-crafting processes, newer 3D printing approaches are being incorporated into practice.[93] Table 2 summarizes six of the most recent publications each for ear, nose, face, eye, and hand prostheses where 3D printing was used. It also briefly summarizes the key details of each article, and states the primary method of 3D printing and materials.

5.1. Craniofacial Prostheses; Ears, Nose, and Face

Craniofacial prostheses include the ears, nose, and adjacent tissue. The highly visible and personal nature of the face means restoring aesthetics and function is critical to a patient's quality of life.[255] It is important, therefore, that polymers and surface coloring match the patient's skin tone, texture, and color detail as closely as possible to merge seamlessly into the natural tissue. They must also possess appropriate mechanical properties to mimic the natural tissue the prosthetic is replacing/substituting.[184] In addition, complex substrates and supporting structures are also required for optimal retention.[264] Medical grade silicone is used in the majority of external (ex vivo) facial prostheses as the main material, although direct 3D printed silicone infiltrated starch prosthetics have also been attempted.[211]

The majority of craniofacial prostheses are fabricated using traditional hand-crafting approaches,[85] although automated 3D scanning, modeling, and 3D printing methods are the subject of much current research to improve the process.[5] Traditional approaches are tedious and time consuming, often requiring physical impressions to be taken, wax prototypes of the prosthesis to be sculpted, and silicone casting using plaster molds. For realism, wax prototypes are often sculpted using tools, such as nylon mesh, bristle brushes, and alcohol torches (**Figure 6**d).[265] 3D printing of craniofacial prostheses require significantly less hand-crafting. The patient's anatomy is captured digitally using medical imaging (e.g., computed tomography),[224,266,267] or 3D scanning methods, such as laser scanning,[266,268] structured light 3D scanning,[269] and photogrammetry.[270,271] A digital model of the prosthetic is then produced using CAD or modeling software.[120,224,267] Commonly, a plastic mold is 3D printed for silicone casting. Direct 3D printing using silicone 3D printers and flexible polymers with silicone-like properties are also available. Nonsilicone direct 3D printing has been evaluated for facial prostheses. For example, a transparent, acrylate-base material ("Tango Plus")[209] printed on the Objet 500 (Stratasys, MN, USA) was used to produce a face prosthetic, however, the tensile and tear strength limits of this material was found to likely result in early prosthesis failure during daily wear and tear compared to silicone.[191] Substructures critical for many facial prostheses can also be designed and fabricated using advanced manufacturing. Craniofacial prosthetics are typically attached to the patient using osseointegrated implants (Figure 6d),[125] or surgical adhesives. Other attachment approaches involve the use of spectacle frames,[272] or hair clips[63] (Figure 6a). Also important for realism is accurate matching of the patient's primary skin color and the addition of microdetails, such as capiliaries, which is the subject of much research.[273,274]

5.2. Prosthetic Eyes

For patients with intact eye sockets, it is common that only an eyeball prosthetic is needed.[275] Otherwise, the soft tissue regions surrounding the eye socket, and in some cases the eye socket itself, also require prosthetic reconstruction to restore aesthetics.[276,277] The greatly different aesthetic and mechanical properties between the eye and adjacent tissue requires the use of multiple materials, including polyurethanes,[278] silicone,[279] and rigid materials, such as acrylic resin.[280] Prosthetic eye attachment is patient dependent, and includes the use of the eye socket, frames of the spectacle, adhesives, or in some cases, osseointegrated implants (Figure 6a). Acrylic resin remains the main prosthetic eye material in use due to its lightweight, strength, versatility and translucency, and ability to be intrinsically and extrinsically colored,[281,282] although silicone methods have also been developed.[283]

Many people who only require eyeball replacement can use standard prostheses.[284] However, these are often mass produced with limited colors and sizes available. Imperfect

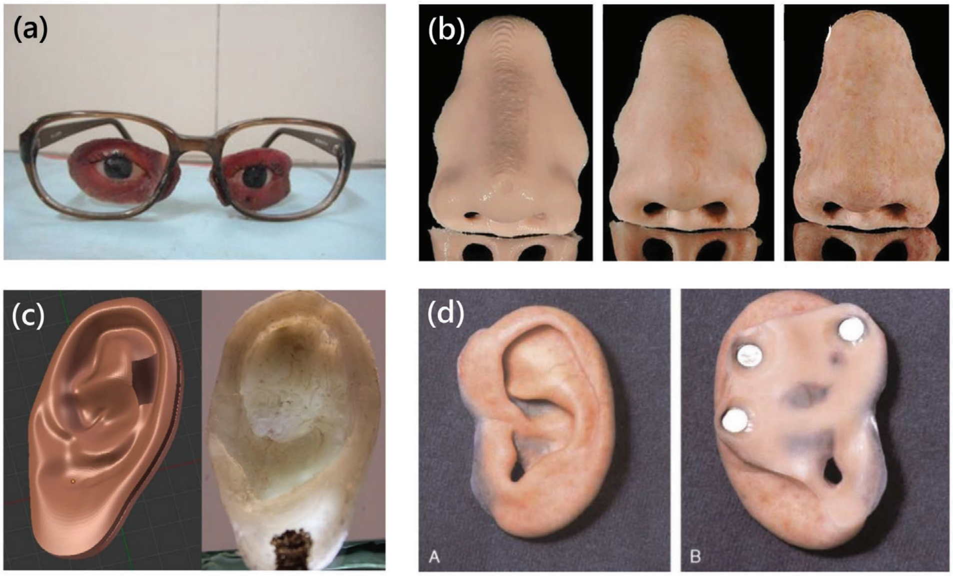

Figure 6. a) Facial prosthesis attachment to spectacles. Reproduced with permission.[316] Copyright 2013, Elsevier. b) 3D printed prosthetic nose before post processing (left), colored and sealed with silicone coating (mid), and polished, sealed with silicone, and colored (right). Reproduced with permission.[4] Copyright 2018, Elsevier. c) An ear prosthesis 3D printed from electroactive poly(vinylidene fluoride); computer model (left), and 3D printed ear (right). Reproduced under the CC-BY Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0).[22] Copyright 2016, The Authors, published by MDPI. d) Auricular prosthesis (left), placement of retaining magnets (right). Reproduced with permission.[322] Copyright 2006, Wolters Kluwer Health, Inc.

size matching can cause irritation and the accumulation of debris and mucous in voids, resulting in the potential of infection.[285,286] This situation can be improved using personalized prostheses that optimally fit the eye socket tissue bed.[286] Impressions of the socket are required; either using a traditional impression device held up against the socket, 3D scanning approaches, or medical imaging methods, such as computed tomography.[287] Although alginate is a commonly used impression material, other materials also available include irreversible hydrocolloid,[286] low-viscosity poly(vinyl siloxane)[288] or silicone-based impression materials.[289] Traditional methods follow the impression stage with a wax pattern which is fitted to the patient and used to form a resin filled mold.[289] Direct 3D printed prototype eyes made from acrylic resion can also be fabricated and trialled in the patient prior to fabrication of the prosthetic eye.[287] Reconstruction of the eye socket and surrounding tissue involves similar processes as with facial prostheses. In many cases, magnetic resonance imaging and computed tomography are used to capture patient morphology,[290,291] although the use of a 3D facial scanner combined with an intraoral scanner has also been employed.[220] Following prosthesis production, aesthetic can be hand painted and coated using a clear acrylic.[286]

5.3. Prosthetic Hands and Fingers

Hand and finger prostheses can include both aesthetic prostheses[292,293] and functional prostheses that include robotic elements that are covered with a cosmetic glove.[294] PVC and silicone are often used for the external materials and can enclose the electronics to make the prosthesis aesthetically pleasing and offer increased protection to the electronics.[294] Aesthetic partial hand prostheses involving only fingers have also been produced.[295] Typical fabrication methodology follows the traditional approach using irreversible hydrocolloid, such as alginate to take an impression of the defected or damaged hand,[64] followed by the positive cast fabrication in dental stone.[292] Final wax models are often hand sculpted based on the shape from an impression of a contralateral finger[292] or from another person.[64,296] Attachment for partial hand and prosthetic fingers includes the use of a glove to fit over the stump,[64,295] implants,[292] or by a ring.[64,297] As with other prosthetics, the most common material for prosthetic fingers is RTV silicone. To improve the appearance and feel of the prosthetic, thickener can be added to the silicone during fabrication.[295,297] Prosthetic fingernails can also be fabricated and often use a heat cured clear acrylic secured using cyanoacrylate or RTV silicone adhesive.[64,296] Although 3D printing approaches have been developed for prosthetics hands, fingers and limbs,[298] the majority of research involves developing solutions to hand and finger motion. This includes low-cost prosthetics hands with limited aesthetics,[299] rigid 3D printed prosthetics to improve function, complex bionic hand prosthetics and the use of flexible 3D printing materials.[298]

5.4. Prosthetic Breasts

For women with a mastectomy, breast tissue restoration can significantly improve their life experience. Sometimes, however, reconstructive surgery is not appropriate and externally worn prosthetic breasts are available.[29] Important considerations for breast prosthesis design include the tactile and dynamic properties compared to natural breasts.[300] Other considerations are weight, how they blend with scar tissue, and the method of retention. Breast prosthesis weight is also important as it impacts both balance and posture, potentially causing injury to the bac and shoulders.[300,301] Due to its natural and soft feel, silicone gel is the most common external prosthetic breast material.[300] Silicone gel prosthesis weight, however, is often one of its main disadvantages.[300] Because of this, alternative designs are being researched, with several patented using polyurethane film for the outer skin.[302,303] Other approaches include a two chamber design surrounded by an outer layer of polyurethane, with one chamber to provide an ideal feel using silicone, and the other chamber containing a light material to reduce weight.[302] Advanced manufacturing has also been used in the fabrication of personalized prosthetic breasts.[304] Using the same approach as with craniofacial prostheses, a 3D scanner captures the torso of the patient before and after mastectomy. A computer model of the contralateral breast is then mirrored, and a two part mold SLS printed using resin. 3D printing using a translucent material means that filling the mold with silicone can be confirmed.[304]

6. Conclusion and Future Outlook

Although advanced manufacturing promises improved prosthetics at reduced costs, traditional approaches still remain predominant in clinical practice. This is due, in part, to the need for practitioners to be trained in digital technologies to encourage the adoption of new innovations.[305] Furthermore, many traditional methods and materials are supported by long-term retrospective studies demonstrating robustness and biocompatibility giving practitioners confidence in their efficacy.[2,65,306,307] Aside from the fabrication process itself, other vital components of the advanced manufacturing pipeline require substantial development, such as 3D scanning and computer modeling. For example, high-accuracy scanners still remain expensive and challenging to use. Frugal approaches using cell-phone cameras are available,[269] however, improvements to their practical usability are still in development.[271] Other drawbacks include the scanning time, up to several minutes, during which the patient may move. This issue is eliminated with multicamera photogrammetry, however, their capital costs are often prohibitive. Modeling software also requires further development to improve its accessibility. Currently available software is not specifically designed for prosthetics and is therefore overly complex with limited usability for design purposes.

In parallel with developments in 3D printing of prosthetics, biofabrication and tissue engineering are also producing exciting results.[263,308] Biofabrication, the application of advanced manufacturing principles to regenerative medicine, involves 3D printing living tissue constructs for surgical implantation.[263] In some cases, this technology has the potential to replace the need for nonpermanent prosthetics. One methodology uses melt electrowriting to fabricate biodegradable porous polymer scaffolds, into which bioinks containing hydrogels and the patient's cells are printed.[263] Following scaffold implantation, new tissue grows within the scaffolds and integrates with existing tissue. Over time, the polymer is resorbed leaving only native tissue. Biofabrication holds much promise, although significant challenges remain before it is ready for use and relatively few clinical trials have been published to date.[308] In one example, patient specific biodegradable scaffolds containing expanded microtia chondrocytes have recently been fabricated. These were cultured in vitro prior to implantation into five microtia patients.[309] Follow-up studies after 2.5 years demonstrated satisfactory aesthetics with the regenerated ears and some evidence of mature cartilage formation. These biofabricated ears, however, did not have the same degree of aesthetic detail as with prosthetic ears.[309] When implemented, biofabrication will reduce the need for manual reconstructive surgery, and in some cases, remove the need for prosthetics. In the near future, it is conceivable that convergences between biofabrication and advanced manufactured prosthetics will lead to hybrid solutions incorporating both living and synthetic components. Developments in 3D printing of prosthetics are also converging with advances in the 3D printing of organic semiconductors and piezoelectric materials (Figure 6c).[24,310,311] Further development of this technology will enable the incorporation of bionics and sensing into the prostheses during fabrication.[22–24,312] Although these have been used in prosthetics for many years, particularly in bionic eyes and bionic limbs, the ability to add this capability during manufacturing will reduce costs and lead to novel solutions that are only possible with advanced manufacturing.[42]

Over the centuries, prosthetics as a science has evolved significantly and we are now at the cross-roads between traditional hand-crafting and advanced manufacturing approaches. Future progress in the art of prosthetics will improve materials and fabrication capabilities, advancing the goal of improving the quality of life for those suffering malformation or tissue loss.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

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