**Title**: Three-Dimensional Printing and Its Applications in Otorhinolaryngology – Head and Neck Surgery

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**ABSTRACT**

*Objective*: Three-dimensional printing technology is being employed in a variety of medical and surgical specialties to improve patient care and advance resident physician training. As the costs of implementing three-dimensional printing have declined, the use of this technology has expanded, especially within surgical specialties. This article explores the types of three-dimensional printing available, highlights the benefits and drawbacks of each methodology, provides examples of how three-dimensional printing has been applied within the field of otolaryngology – head and neck surgery, discusses future innovations, and explores the financial impact of these advances.

*Data Sources*: Articles were identified from PubMed and Ovid Medline.

*Review Methods*: PubMed and Ovid Medline were queried for English articles published between 2011and 2016, including a few articles prior to this time as relevant examples. Search terms included: three-dimensional printing, 3D-printing, otolaryngology, additive manufacturing, craniofacial, reconstruction, temporal bone, airway, sinus, cost, and anatomic models.

*Conclusions*: Three-dimensional printing has been used in recent years in otolaryngology for preoperative planning, education, prostheses, grafting, and reconstruction. Emerging technologies include the printing of tissue scaffolds for the auricle and nose, more realistic training models, and personalized implantable medical devices.

*Implications for Practice*: After accounting for the upfront costs of three-dimensional printing, its utilization in surgical models, patient-specific implants, and custom instruments can reduce operating room time and thus decrease costs. Educational and training models provide an opportunity to better visualize anomalies, practice surgical technique, predict problems that might arise, and improve quality by reducing mistakes.

## INTRODUCTION

Ongoing rapid technological advancements have challenged the medical field to assimilate new technologies at an ever-increasing speed. Three-dimensional (3D)-printing, also referred to as rapid prototyping, solid-freeform technology, or additive manufacturing, represents a technology still in the nascent stages of adaptation by the medical field[1]. Early developments in 3D-printing occurred in the 1980s, and its employment across many industries followed as a result of its ability to quickly produce customizable materials for individualized purposes[1]. Recently, these same characteristics have provided great appeal for medical and surgical applications. Customization offers the potential to create patient specific objects. Coupled with advances in material sciences, this has allowed these items to be implanted within the human body with reduced rejection or infection risks[2].

Numerous medical and surgical specialties have explored 3D-printing to model pathology, plan procedures, and manufacture educational models. The literature surrounding these developments continues to grow (**Figure 1**). Many of these articles relate to plastic surgery and craniofacial reconstruction involving the skull base, orbital floor, mandible and maxilla[3]. With potential head and neck surgery applications, it is not surprising that 3D-printing has been utilized by plastic surgeons, oral and maxillofacial surgeons, maxillofacial prosthodontists and anaplastologists. To date, however, there is a relative paucity of literature addressing the uses of 3D-printing specific to otolaryngology. Indeed, many related and shared applications exist, but there remains the untapped potential for more applications exclusive to otolaryngology. 3D-printing provides an intuitive solution for preoperative planning and surgical training within otologic, rhinologic, and laryngologic anatomy. Recent otolaryngology applications have been described, yet to date no comprehensive review of the uses of 3D-printing in this field exists.

This review explores current techniques in 3D-printing, potential applications to otolaryngology, logistical and fiscal limitations, and future possibilities.

## METHODS

Electronic database searches using Ovid Medline and PubMed were performed utilizing Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, excluding sources published before January 2011 through June 2016 in order to provide readers with the most current information and comply with state-of-the-art review criteria. Select articles published earlier were included when relevant information was presented. Because of the manageable number of results, automatic term mapping was utilized without specific Medical Subject Heading (MeSH) modifiers. Only English language articles were included. Searches were performed independently by two authors (TDC and SEE) using relevant keywords including: 3D-printing, three-dimensional printing, otolaryngology, additive manufacturing, craniofacial, reconstruction, temporal bone, airway, sinus, cost, and anatomic models. Additional searches were performed to include articles relevant to related surgical subspecialties such as plastic surgery and neurosurgery where overlap with otolaryngology existed. Articles were included which detailed 3D-printing developments or applications for procedures and pathologies either directly related or clinically similar to the practice of otolaryngology. Those studies with applications unique to other subspecialties were excluded. More recent articles were favored over more dated publications. Additional articles were extracted by reviewing sources of the most relevant articles. The decision to include or exclude equivocal articles was decided by two authors (TDC and SEE; see **Figure 2**).

## DISCUSSION

### Three-Dimensional Modeling

The process of printing a 3D-object begins with the utilization of computer-aided design (CAD) software to create a virtual prototype. Several CAD programs allow users to render 3D-models and export them as files which are compatible with 3D-printers[1]. One of the most common types is the ".STL" file. While this name refers to "stereolithography," it is also sometimes called "standard triangle language" or "standard tessellation language."[4] CAD programs are often used to design objects *de novo* which can be translated into a printable prototype before eventual individual or large-scale production.

Recent advances in software technology, however, have yielded opportunities for overcoming challenges. By employing post-processing algorithms, spatial model data can be generated from local computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US) images[5,6]. Raw data sets for these modalities are stored in the Digital Imaging and Communications in Medicine (DICOM) format. CAD programs generate printable 3D-models from DICOM data. First, the computer software selects pertinent portions of the image to undergo extraction, or so-called "segmentation," followed by selective editing[6]. During segmentation, the desired area or volume of the radiographic image is delineated to be individually selected and isolated for use. Several selection methods exist; the portion can be manually outlined by the user or more complex algorithms can be employed which allow for automatic selection based on the characteristics of individual pixels[7]. After this, volumetric data is converted to a 3D-triangular mesh and exported as a .STL file[5]. 3D-printers can then use this data to create patient-individualized objects (**Figure 3**).

Standardized steps in the production process allow for critical collaboration among scientists worldwide. Printing parameters can be shared via .STL files uploaded to public databases such as the National Institutes of Health's (NIH) 3D-Print Exchange (3dprint.nih.gov) to promote collaboration between researchers. This is similar to anatomic models, lab instruments, and the structures of protein, viruses, and microorganisms that are currently available for download and production through the NIH[8].

As 3D-printing creates solid objects layer-by-layer, fabrication begins from the base of the object and finishes at the top. CAD modeling guides the way each layer is dispersed[1]. Thus, the resolution or intricacy of each technique depends not only on the ability to distribute, polymerize, and revise printed materials, but also on the quality of CAD data utilized. The more intricate a desired structural model is, the more radiographic data is required[5]. In maxillofacial modeling from CT imaging, slice thickness should be between 0.5-1mm which is consistent with the majority of high resolution (1mm cuts) maxillofacial CT scans[9].

3D-printing represents a generalized term encompassing multiple techniques for creating an object from software design or radiographic data. Over the past several decades, printing processes have evolved and differentiated to provide optimal solutions for diverse needs. Each 3D-printing type exemplifies different material requirements, costs, and efficacy[1]. In order to provide a more comprehensive overview of 3D-printing processes, a few of the most commonly used techniques are discussed below and summarized in **Table 1**.

*Stereolithography*

Despite being the first 3D-printing process developed, stereolithography (SLA) remains the industry's gold standard[5,10]. SLA involves vat photopolymerization dependent on the exposure of liquid resins to ultraviolet (UV)-light generated by a moving CAD-controlled UV-source. Free radicals generated by UV-radiation drive the resin into the solid phase[11]. Afterward, additional processing is needed to remove leftover resin and support structures before final UV-chamber curing. SLA can produce incredibly high-resolution entities; however, the overall process is slow and materials may be costly relative to other 3D-printing methods[10].

Continuous liquid interface production (CLIP) represents a recent advancement in SLA where the fabricated object is pulled from a liquid resin pool[10,12]. Liquid resin continually fills in below the extracted object and resin exposure to UV-light passing through an oxygen permeable window allows uninterrupted production and high resolution. Proper development of these capabilities has the potential to reduce both the time and cost of stereolithographic 3D-printing[12].

*Material Jetting Printing*

Material jetting printing (MJP) differs from SLA in its immobile UV-source. In addition, fabrication is contingent upon the positional deposition of liquid resin[10]. It shares many similarities with conventional 2D-inkjet printers, except that it utilizes photopolymerization resins and printing proceeds along the vertical axis. Numerous styles of MJP machines are available with the two fundamental types of jetting being continuous and drop on demand[1]. When compared to SLA, MJP holds several distinct advantages despite added expense. The most notable is compositional control; by dispensing individual drops of resin, materials can be adjusted during the printing process. This allows for the production of heterogeneous objects with the added possibility of material gradients and extremely high resolution[13]. Furthermore, the UV-source continually fixes the resin as it deposits and thus results in reduced post-production processing[10].

*Binder Jetting Printing*

Binder jetting printing (BJP) differs from the above methods in that it uses a powder base in addition to a binder substance. Compatible materials added after drying the binder and powder include metals, glass, and sand. BJP requires a substantial amount of processing after all layers have been fabricated. The object must undergo de-powdering and sintering, where it is heated to improve its mechanical properties. Then, it is infiltrated with additional materials and annealed to improve its structural integrity before finishing. These steps require both extra materials to strengthen the object and manual labor[14]. Despite the added post-processing time, BJP remains a relatively expedient form of 3D-printing. The machinery also has the added benefits of being relatively small and quiet. While BJP claims several advantages, its relatively inferior resolution capabilities are one noted disadvantage[15].

*Selective Laser Sintering*

Similar to BJP, selective laser sintering (SLS) relies on the alteration of deposited powder. The final object is formed by repeated layers of powder deposition and laser sintering to melt and fuse the powder[1]. Related types of powder bed fusion include direct metal laser sintering, electron beam melting, and selective heat sintering. Because it utilizes powder as the basis for production, several materials are available for sintering including polymers, nylon, resin, metal, and ceramics. As with BJP, SLS also requires more extensive post-production processing. One significant advantage of SLS is its ability to produce soft scaffolding, conducive for soft tissue uses[16]. Use of the laser apparatus requires a highly experienced operator and special facilities, which make it more expensive and less feasible for local medical applications[10].

*Fused Deposition Modeling*

Fused deposition modeling (FDM) relies on material to be injected directly onto the fabrication platform without interacting with a powder or binding substance. The material must be heated to a semi-molten state and extruded through nozzles where it solidifies as the platform moves vertically to repeat the process for each layer[1]. FDM is generally less expensive than other 3D-printing methods by a substantial margin[10]. FDM is less limited by the availability of materials; even metals and ceramics can be used[1]. Thermoplastic substances must be pliable enough to be extruded but also viscous enough to maintain shape after deposition[16]. It should be noted that FDM is not capable of integrating as many different materials as other forms of printing and demonstrates relatively poor resolution and surface finish[1,10].

## **Applications in Otorhinolaryngology**

A comprehensive listing of literature from the last five years highlighting uses of 3D-printing relevant to otorhinolaryngology – head and neck surgery is presented in **Table 2**.

*Perioperative Planning & Patient Education*

The ability to quickly and accurately fabricate models of complex anatomical structures has dramatically improved the way many surgeons preoperatively plan. Instead of relying only on 2D-radiologic imaging, full-scale 3D-replicas of pertinent structures with the added benefit of tactile feedback are now possible. Studies in multiple specialties have already demonstrated 3D-printing's utility in soft tissue, vascular, and bony tissue mapping[10]. 3D-modeling and manufacturing help practitioners visualize anatomy preoperatively, practice techniques, anticipate errors, reduce guesswork, predict results, and minimize duration of operations[17]. Customized surgical templates and equipment further optimize operative interventions[10].

For instance, 3D-printed model templates are used to bend plates for mandibular reconstruction in the preoperative period so that this process does not demand operative time while under general anesthesia[17]. Mandibular reconstruction represents greater complexity because of load bearing and occlusive requirements. 3D-printing allows for precise mandibular reconstruction planning, preparation of surgical implants, and the manufacturing of dental prostheses[17]. Similar benefits have been noted in maxillary reconstructions where the alignment of titanium meshes can be checked against printed replications[18]. Titanium implants created from 3D-rendered molds have been shown to provide an accurate fit with reduced need for corrective surgery[5]. Preoperative planning and device customization have had such an impact on reducing operative duration that mandibular ablation, reconstruction, dental implantation, and dental prostheses placement can all be accomplished in a single-stage[19]. 3D-printing customizable instrumentation is another interesting possibility. For example, 3D-printed laryngoscopes have allowed surgeons to utilize intraoperative surgical imaging for transoral surgery where traditional metal instruments would prohibit the use of MRI and produce significant artifact on CT[20].

A number of articles also describe the use of 3D-printing for preoperative surgical feasibility and mapping. In one example, a 3D-printed skull model was successfully used to plan the resection of a skull base juvenile nasopharyngeal angiofibroma[21]. Other skull base pathologies, such as petroclival tumors, have been mapped out preoperatively with 3D-printed models to evaluate access and tumor exposure[22]. In another study evaluating frontal sinus mapping during osteoplastic flap approaches, 3D-printed models were used as onlay guides shown to be accurate to within 1mm[23]. 3D-printed replicas have also assisted with the planning of technically challenging otologic surgeries on the pediatric temporal bone[24]. Another report highlights how a personalized replica of the auricle was 3D-printed with an acrylonitrile butadiene styrene resin in order to assist in the preoperative planning of ear reconstruction[25].

3D-printing also has important implications for *in utero* evaluation of congenital defects. Anomalies of neck and maxillofacial structures have the potential to obstruct the neonatal airway, complicating postpartum management. In these cases, *ex utero* intrapartum treatment (EXIT) procedures can optimize fetal oxygenation while securing the airway. However, such drastic intervention can be avoided if confirmation of airway patency can be obtained *in utero*. Previously, fetal MRI datasets have been used to generate virtual 3D-models of bronchial trees to assess for obstruction, but only recently did the first case report describe a physical model being used to assess airway patency[26,27]. The authors created a printed 3D-model of fetus' maxillofacial defect from MRI data which demonstrated no functional limitations in the airway. The infant was delivered without significant perinatal intervention, thereby avoiding the cost and ameliorating the potential morbidity of an EXIT procedure[26].

Finally, 3D-models of anatomical structures can also be useful for patient education. By being able to interact both visually and physically with these models, patients can better understand pathologies and interventions without having to navigate the complexities of radiographic imaging. The added ease and comfort associated with a visually-relatable model may intuitively aid in streamlining the surgical consent process[10]. A combination of pre-operative and projected post-operative models may also be used to provide patients with a realistic 3D-outcome to better manage expectations especially in the areas of facial plastics and reconstruction[28].

*Surgical Training*

3D-printing can be integrated into resident education where it is often difficult and inefficient to teach specialized surgical skills to first time learners in the operating room. This technology enables physician learners to practice these skills while lessening the danger to patients through the use of complex high fidelity models[29]. For example, multiple centers have reported data on 3D-printed temporal bones in the education of their trainees[29-31]. During implementation, participants were asked to qualitatively evaluate these training exercises in terms of realism, anatomical accuracy, utility, and efficacy. Despite using different materials in the 3D-printing process, results were largely similar with positive feedback from trainees[29-31]. 3D-printed temporal bones would obviate the need for acquiring and harvesting temporal bones from cadaveric donors, but limitations include difficulty replicating middle ear bones and retained powders within mastoid air cells[32,33].

The use of educational models for training endoscopic techniques also shows significant promise. Patient radiographic image derived 3D-printed models have been designed to mimic anterior skull base pathologies, allowing trainees to practice drilling via an endonasal approach with no risk to patients – a skill some trainees may rarely have the opportunity to practice[34,35]. Authors have found 3D-printed models to be both effective and realistic training modalities for thispurpose [36]. 3D-models of the tracheobronchial tree can realistically simulate bronchoscopy and introduce anatomical variants that may otherwise be only rarely encountered[37].

Similarly, 3D-printed cricoid cartilage models have been used for training with balloon dilation. This allows surgeons and trainees to get a feel for the resistance of the airway before attempting balloon dilation. It also allows measurement of the force that will fracture the cricoid cartilage and can help set parameters for human use[38]. At another institution, 3D-printed starch:silicone composite was found to closely mimic costochondral cartilage and offered a useful alternative for training resident surgeons to practice carving pediatric costal cartilages for complicated microtia repair[39].

Educational uses are likely to be the most rapidly integrated by otolaryngology in the future. Models can be printed with specific pathologies and anomalies to best prepare for a specific operation. This can increase exposure to rare pathologies that residents may not otherwise encounter in their training. Training models such as the Electric Phantom (ElePhant) allow for training with real-time feedback. ElePhant utilizes 3D-printed models with vital structures (e.g. facial nerve) replaced with either a conductive alloy or fiberoptic material; inadvertent trauma alerts the user thus providing immediate feedback. The amount of structural damage and predicted patient deficits are noted, allowing residents to make mistakes on models rather than patients[40].

*Grafting, Prostheses, and Reconstruction*

The surgical management of the pediatric and adult airway provides an intriguing opportunity for 3D-printing. Multiple centers have investigated the use of biomaterial grafts in animal models, and a recent publication highlighted 3D-printed biocompatible scaffold synthesis. Tracheal chondrocytes were cultured on the scaffold to create a graft used in rabbits undergoing laryngotracheal reconstruction. Chondrocyte grafts demonstrated successful viability in a large majority of these subjects[41]. A similar study with 3D-printed polycaprolactone (PCL) grafts coated with human turbinate mesenchymal stromal cells showed that these materials are capable of producing superior tracheal epithelial regeneration[42]. Beyond epithelial grafting, 3D-printing has been used in the production of related structures, such as the trachea itself. Mesenchymal stem cells have been used with 3D-printed PCL scaffolds to create implantable structures which maintain the luminal shape and function of the trachea in rabbits[43]. Furthermore, *in vitro* work on the development of a 3D-printed tissue-engineered trachea has demonstrated a dramatic capacity for regeneration and realistic mechanical qualities[44]. Others have 3D-printed esophageal patches for use in rabbit models which may pave the way for esophageal replacement rather than relying on gastric pull-up techniques after esophagectomy in humans[45].

The prospective benefit of 3D-printing in the airway has also been illustrated in human patients through the creation of resorbable airway splints for life-threatening tracheobronchomalacia. The 3D-printed PCL splint was sewn into the left main bronchus which dramatically improved pulmonary status allowing vent-weaning and eventual patient discharge[46]. Retrospective results from this and two other patients were later published with cited immediate benefits in oxygenation and airway growth noted in each child; this improvement was maintained throughout follow up over several years[47]. At the same institution, a prospective clinical trial evaluating custom 3D-printed continuous positive airway pressure (CPAP) masks for pediatric obstructive sleep apnea (OSA) patients with craniofacial anomalies is currently being evaluated[48].

Another area where 3D-printing may prove useful is in the synthesis of implantable structural tissues. This is particularly true in facial plastics and reconstruction where functional and aesthetic outcomes are paramount[49]. In a recent mouse model study, artificial nasal alar cartilage was fabricated from the 3D-printing of gum resin[50]. In the future, such structures could be used in conjunction with human cells to reconstruct the nasal cartilaginous skeleton. Similar work has been done for auricular reconstruction to determine the feasibility of creating a customized ear implant using 3D-printing[51]. One group 3D-printed tympanic membrane grafts which were found to better resist deformation than temporalis fascia and obviated the need for additional skin incisions and time for fascia harvesting[52]. In a recent study, the same group 3D-printed custom prostheses to successfully repair superior semicircular canal dehiscence in cadavers[53].

One of the most exciting prospects for the development of 3D-printing techniques is for complex head and neck reconstructive surgeries. With such intricate and lengthy operations, the creation of models and prostheses may reduce operating time, potentially reducing blood loss, wound exposure, and duration of anesthesia[54]. While planning for difficult free flap reconstructions, 3D-printing may be utilized to insure adequate coverage of a defect and reasonable proximity to a vascular supply[55]. Although 3D-printing was utilized more often to create molds for titanium implants, full mandibles may now be 3D-printed and successfully implanted in patients[2]. 3D-printed implants have been developed using polymers such as silicone, polymethylmethacrylate, and polyetheretherketone which are biocompatible[56]. Several others have utilized α–tricalcium phosphate to 3D-print customized artificial bones which were successfully implanted in patients undergoing maxillofacial reconstructions[57,58]. Additionally, 3D-printing has been used to create a customized tray made from hydroxyapatite/poly-L-lactide, which aids in the inset of a fibular free flap similar to the marketed "V-stand" type guides[59,60]. 3D-printing has also been used to create molds for custom-designed anatomic spacers and prostheses required for temporomandibular joint reconstruction[61,62]. Recent animal models have demonstrated promise with 3D-printed osseoconductive scaffolds which allow bone ingrowth to replace craniofacial defects, possibly obviating the need for autogenous osseous flap harvest[63].

Currently, many otolaryngologic applications for 3D-printing are at preliminary stages of development. Many have only been evaluated in animal models or in proof-of-concept reports. Those referenced in this paper that are being evaluated in clinical practice include printed mandibles for reconstruction and resorbable laryngeal stents, in addition to CPAP masks currently undergoing clinical trials[17,46,47]. The FDA reports having approved over 85 3D-printed devices, including surgical instruments and dental restorations (see: http://www.fda.gov). With increased focus on potential applications for the field, there may well be further investigations in human subjects.

## IMPLICATIONS FOR PRACTICE

### *Limitations*

The belief that upfront investment costs to implement 3D-printing are prohibitive likely remains a deterrent to its wider utilization within otolaryngology. Prices continue to decline, however, and there is evidence that using 3D-printed materials can be a cost saving measure[64]. For medical purposes, there remains a limited number of FDA approved materials which results in higher material costs. While the materials used to 3D-print educational models are becoming more and more accessible, many educators have ongoing concerns that no true substitute exists for human tissue. The use of 3D-printed models, however, potentially reduces reliance on the acquisition of cadaveric bone. Research has shown that these models are an acceptable alternative[29-31].

Other concerns with 3D-printing implementation include the time required to obtain proper imaging formats, dedicated personnel for printer programming and troubleshooting, and the physical space and time required for printing high fidelity models. As 3D-printing technology has improved, the printing time requirement has been reduced significantly. In one study, fifty auricular and nasal scaffolds were printed within four to five hours[65]. In another study, 3D-printing half a skull took just under 14 hours including preprocessing, printing, and post-processing[66]. The amount of post-processing required to remove excess material and smooth down edges varies depending on the type of printer and substrate but is not negligible[5]. One aspect of 3D-printing which may significantly slow its implementation is the time needed to become proficient with CAD design and print-planning. The ability to produce medical quality 3D-objects requires the experience obtained by trial and error with the CAD software. Even with decreasing overall production times, pre-surgical 3D-printing is not presently applicable in truly emergent situations[67].

It should also be noted that a large portion of the articles published to date, including many presented in this manuscript, are proof-of-concept and have not been validated by large-scale studies or randomized control trials. While the potential implications of these individual case reports and small series are encouraging, caution should be exercised in interpreting the current impact, cost effectiveness, or future use of 3D-printing in clinical practice. Furthermore, the large range of 3D-printing applications currently utilized are so varied, and in such different stages of development, that drawing comparisons between them would be unreasonable at this time.

*Cost Considerations*

As 3D-printing is more widely utilized in medicine, the market is predicted to generate $4.038 billion by 2018[68]. Although the costs associated with 3D-printing are gradually declining, the initial investment to cover the printer, software, and materials remains a significant hurdle to implementing 3D-printing in academic and private medical settings. The cost of 3D-printers can range from $200 for simple desktop devices to more than $250,000 for bioprinters that can print living cells (see: http://www.aniwaa.com/). A 1 kilogram (kg) spool of polylactic acid (PLA) 1.75mm printing filament can be purchased for as low as $19.99 and printing model skulls and temporal bones can be achieved for as little as $1-5 per skull and less than $30 per temporal bone[32,66].

In a review of 158 articles evaluating 3D-printing in surgery, researchers are split between those who believe that the costs associated with 3D-printing are an advantage over conventional methods (n = 24; 15.2%) versus those who feel that the costs of equipment and cost per patient is a disadvantage (n = 30; 19%)[64].

One reported cost saving measure by proponents of 3D-printing use is decreased operating time. Estimates of operating time per minute can rise to $100, thus utilizing 3D-printing technology can save an average of 25.2 minutes per procedure[64,68]. However, to date there have not been any randomized, controlled trials to evaluate whether 3D-printing can significantly reduce operating times[5].

Another cost saving measure is the in-house printing of surgical instruments such as retractors. This can be done at a discounted rate compared to purchasing stainless-steel alternatives from a bulk supplier, and instruments can be printed in an optimal size or dimension to fit the situation[67]. PLA is a commonly utilized material which can be sterilized and reused while withstanding enough force to retract human tissues during surgery[69]. If costs still remain an issue, collaboration may be the solution. At academic medical centers it is possible to share both 3D-printers and the required software among several departments.

*Future Applications*

3D-printing has allowed for incredible advances, but concern remains that some of the claims may be overstated. Tissue scaffolds and bioprinting of skin have been major breakthroughs in recent years, but many of the proposed technologies, including organ printing, are still years away[8,65,70]. Early animal models have shown promise for auricular and nasal scaffolding; 3D-printed implantable models are being evaluated.[65] These scaffolds maintained an adequate anatomical structure, and histological appearance showed cartilaginous growth within the confines of the scaffold. This technology could one day replace rib and calvarial bone harvesting in auricular and nasal reconstruction.[65]

The biggest obstacle to organ printing is the need to elaborate a vascular network to deliver oxygen and remove waste[71]. 3D-printing allows vascular structures to be constructed from biomaterials, which can later be seeded with endothelial cells[72,73]. Vessel-like microfluidic channels flanked by tissue spheroids have also been proposed and may be a viable option in the future. Other steps required to achieve organ production include the isolation and differentiation of stem cells, preparation and loading of cells in a support medium, bioprinting, and organogenesis in a bioreactor[71]. Some progress has been made toward this end, with one study reporting the three-dimensional printing of multiple bioinks to generate complex structures, including vasculature, extracellular matrix, and multiple types of surrounding cells[74]. At the same institution success was demonstrated in creating tissues more than 1cm thick, which were able to be perfused on chips for six weeks[75].

More complex tissue and organ production could be useful in correcting congenital anomalies, reconstructing cancerous defects, and rebuilding traumatic avulsing injuries[71]. Vascular pathologies, such as arteriovenous malformations, can be created as well[76]. In otolaryngology, this may ultimately include the ossicles, cochlear and vestibular structures, turbinates, and laryngeal subunits, to name a few. Although issues with rejection can still occur with 3D-printing, autologous tissue or stem cell sources can reduce the likelihood of complications[71].

Further integration of 3D-printing technologies has the potential to generate improvements in patient care, surgical outcomes, and resident education. While upfront costs remain a concern in purchasing discussions, interdepartmental collaborations at academic centers can mitigate these costs and expand access to this innovative technology. 3D-printing may improve how residents are trained in surgical approaches to the anterior and lateral skull base, how the airway is stented and reconstructed, and how osseous and soft tissue defects of the face, head, and neck are reconstructed. Leaders in otolaryngology – head and neck surgery should give serious consideration to investing in and expanding the use of 3D-printing technology to improve future resident training and patient outcomes.

## Disclosures

The authors have no disclosures, financial interests, or other conflicts of interest.

## IRB Attestation

Non-human subjects research involving literature review alone does not require review by the Indiana University Institutional Review Board according to the Office of Research Compliance regulations.


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**Table 1**: Comparison of various 3D-printing methodologies.

| Type | Composition | Process | Advantages | Disadvantages | Cost |
|---|---|---|---|---|---|
| **SLA** | Liquid resin | -Polymerization requires exposure to UV-light | -Current gold standard<br>-High resolution 0.025 mm | -Req. post-production processing<br>-Print times > 1day<br>-Can only use one resin at a time | -Some materials quite costly<br>-Printer maintenance is also costly |
| **CLIP** | Liquid resin | -Fabricated object pulled from liquid resin pool<br>-Faster than SLA | -Resolution below 100 micrometers<br>-Can use multiple materials | -Similar to SLA | -Similar to SLA |
| **MJP** | Liquid resin | -Photopolymerizes<br>-Continuous or Drop on Demand | -Heterogeneous objects possible<br>-Resolution < 20 nm<br>-Less printer maintenance | -Can only utilize materials in droplet form | -Printer is more expensive relative to other methods |
| **BJP** | Powder base and printed binder substance | -Layer of binder applied to powder surface and dried under heater<br>-Additional layers added and dried until object completed | -Can print multiple colors/materials<br>-Small, quiet printer<br>-Can create multiple objects in one day | -Requires a substantial amount of post-processing<br>-Final product has rough finish and less strength than SLA; must be reinforced<br>-Inferior resolution capabilities | -Printers are much more affordable than other types |
| **SLS** | Powder materials | -Laser source applied in a specific pattern to heat powder<br>-Repeated layers of powder deposition and laser sintering | -Can use many materials including metals, ceramic, nylon, polycarbonate, etc.<br>-Does not require binding liquid<br>-Un-sintered powders can be reused | -Resolution limited by powder particle size<br>-Laser requires highly experienced operator and special facilities<br>-Unused powders must be brushed away from final product<br>-Models may suffer shrinkage | -Expensive due to initial cost of printer and specialized required equipment |
| **FDM** | Solid thermoplastic filaments | -Molten state released through nozzle then re-solidifies<br>-Moves vertically to add layers | -Most affordable<br>-Most commonly used consumer product<br>-Practical for desktop use | -Materials must have proper viscosity<br>-Cannot produce heterogeneous materials as well as other methods<br>-Low resolution | -Less expensive than other methods due to decreased maintenance and print material costs |

SLA = stereolithography, CLIP = continuous liquid interface production, MJP = material jetting,

BJP = binder jetting printing, SLS = selective laser sintering,

FDM = fusion deposition modeling, mm = millimeters; nm = nanometers

**Table 2**: Publications relevant to 3D-printing in otolaryngology – head and neck surgery.

| Source | Subspecialty | Application Type | Publication | Explored utility |
|---|---|---|---|---|
| **Berens et al. 2016**[39] | Pediatrics | Preoperative planning, education | Study | Auricular chondral framework model |
| **Cho et al. 2016**[55] | Facial Plastics/Recon | Preoperative planning | Case report | Preoperative flap design to ensure adequate tissue mobility/coverage |
| **Gray et al. 2016**[49] | Facial Plastics/Recon | Preoperative planning | Study | Nasal models (estimate nasal tip reaction force) |
| **Green et al. 2016**[61] | Facial Plastics/Recon | Prosthesis | Case series | Temporomandibular joint spacer |
| **Johnson et al. 2016**[38] | Pediatrics | Education | Study | 3D-printed cricoid cartilage compared to cadaver cartilage |
| **Kozin et al. 2016**[52] | Facial Plastics/Recon | Prostheses/Recon | Study | Tympanic membrane grafts |
| **Muelleman et al. 2016**[22] | Otology/Neurotology | Preoperative planning | Case series | Skull base petroclival tumor models |
| **Park et al. 2016**[45] | Head & Neck | Prostheses/Recon | Study | Tissue-engineered esophagus graft *in vivo* animal model |
| **Ryu J et al. 2016**[62] | Facial Plastics/Recon | Preoperative planning, implants | Case Report | Customized bilateral temporomandibular joint replacement |
| **Bos et al. 2015**[51] | Facial Plastics/Recon | Prostheses/Recon | Study | Ear implant models (compared cadaveric & 3D-printed ears) |
| **Chae et al. 2015**[10] | Facial Plastics/Recon | Preoperative planning, education | Review (Plastics Literature) | Highlights numerous soft tissue, bony, & vascular flap mapping |
| **Cohen & Reyes 2015**[32] | Otology/Neurotology | Education | Study | 3D-printed temporal bone models produced from CT |
| **Da Cruz & Francis 2015**[30] | Otology/Neurotology | Education | Study | Inexpensive temporal bone models |
| **Goldstein et al. 2015**[41] | Pediatrics | Biologic implants | Study | Tissue-engineered airway graft *in vivo* animal model |
| **Hochman et al. 2015**[31] | Otology/Neurotology | Education | Study | Temporal bone lab models |
| **Kozin et al. 2015**[53] | Otology/Neurotology | Prosthesis | Study | 3D-printed custom prostheses to repair superior circular canal defects |
| **Morrison et al. 2015**[47] | Pediatrics | Prosthesis | Case series | External airway splints for tracheo- and bronchomalacia |
| **Mowry et al. 2015**[33] | Otology/Neurotology | Education | Study | Temporal bone models created from desktop 3D-printers |

| | | | | |
|---|---|---|---|---|
| **Narayanan et al. 2015[35]** | Rhinology / Skull Base | Education | Study | Anterior skull base pathology model |
| **Park et al. 2015[44]** | Head & Neck | Prostheses/Recon | Study | Tissue-engineered trachea |
| **Park et al. 2015[42]** | Head & Neck | Prostheses/Recon | Study | Tissue-engineered tracheal graft using turbinate stem cells |
| **Reiser et al. 2015[60]** | Facial Plastics/Recon | Preoperative/ intraoperative planning | Prospective cohort study | V-stand lower mandible template |
| **Rose et al. 2015[29]** | Otology/Neurotology | Preoperative planning, education | Study | Multi-material temporal bone models |
| **Rose et al. 2015[24]** | Otology/Neurotology | Preoperative planning | Case report | Abnormal pediatric temporal bone model |
| **Shan et al. 2015[18]** | Facial Plastics/Recon | Prostheses/Recon | Prospective cohort study | Mandibular/maxillary titanium meshes |
| **VanKoevering et al. 2015[26]** | Pediatrics | Preoperative planning | Case report | Fetal craniofacial anatomic model |
| **Waran et al. 2015[36]** | Rhinology / Skull Base | Education | Study | 3D-models for endoscopic approaches |
| **Xu et al. 2015[50]** | Facial Plastics/Recon | Prostheses/Recon | Study | Tissue-engineered nasal alar cartilage *in vivo* mouse model |
| **Zopf et al. 2015[65]** | Facial Plastics/Recon | Implants/Reconstruction | Study | Porous tissue bioscaffolds for soft tissue reconstruction |
| **Chang et al. 2014[43]** | Otolaryngology | Prostheses/Recon | Study | Tissue-engineered tracheal graft *in vivo* rabbit model |
| **Nishimoto et al. 2014[25]** | Otolaryngology | Preoperative planning | Case report | Auricular chondral framework model |
| **Levine et al. 2013[19]** | Plastic surgery | Preoperative planning | Case series | Surgical device/guide |
| **Werner et al. 2013[27]** | Pediatrics | Preoperative planning | Case series | Fetal airway model |
| **Zopf et al. 2013[46]** | Pediatrics | Prosthesis | Case report | Bioresorbable airway splint for tracheo-bronchomalacia |
| **Patel et al. 2012[17]** | Facial Plastics/Recon | Preoperative planning | Case series | Mandible templates |
| **Ricci et al. 2012[63]** | Facial Plastics/Recon | Prostheses/Recon | Study | Osseoconductive graft lattices |
| **Daniel et al. 2011[23]** | Rhinology / Skull Base | Preoperative/intraoperative planning | Case series | Frontal sinus models and onlay templates |

3D = three-dimensional; CT = comuted tomography

**Figure Legends**:

**Figure 1**: Number of all publications found in PubMed resulting from query for "3D printing" available by year from 1990 to 2015. Additional sources may exist from alternative database searches unavailable through PubMed .

**Figure 2**: PRISMA flow diagram of the literature review process evaluating 3D-printing in otorhinolaryngology – head and neck surgery.

**Figure 3**: Flow diagram showing the step-wise process of 3D-printing an educational model. Model obtained from open source website (http://www.thingiverse.com/thing:1362802) and printed at our institution.

CT = computed tomography, MRI = magnetic resonance imaging, US = ultrasound,

DICOM = digital imaging and communications in medicine, CAD = computer aided design,

3D = three dimensional, .STL = standard tessellation language

Number of 3D-Printing Publications in PubMed by Year
800
700
600
500
400
300
200
100
0
3
1
0
1
2
0
2
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3
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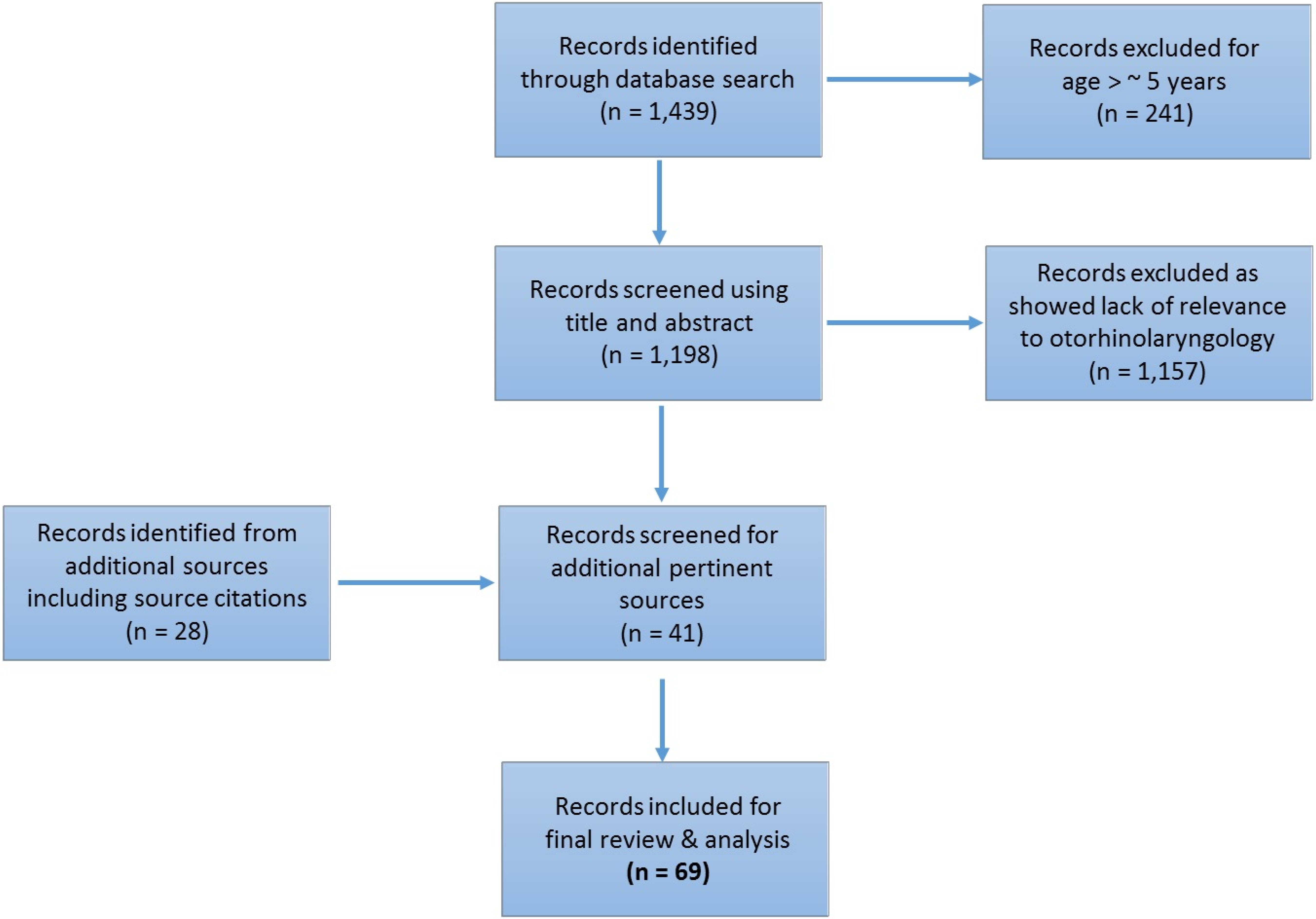
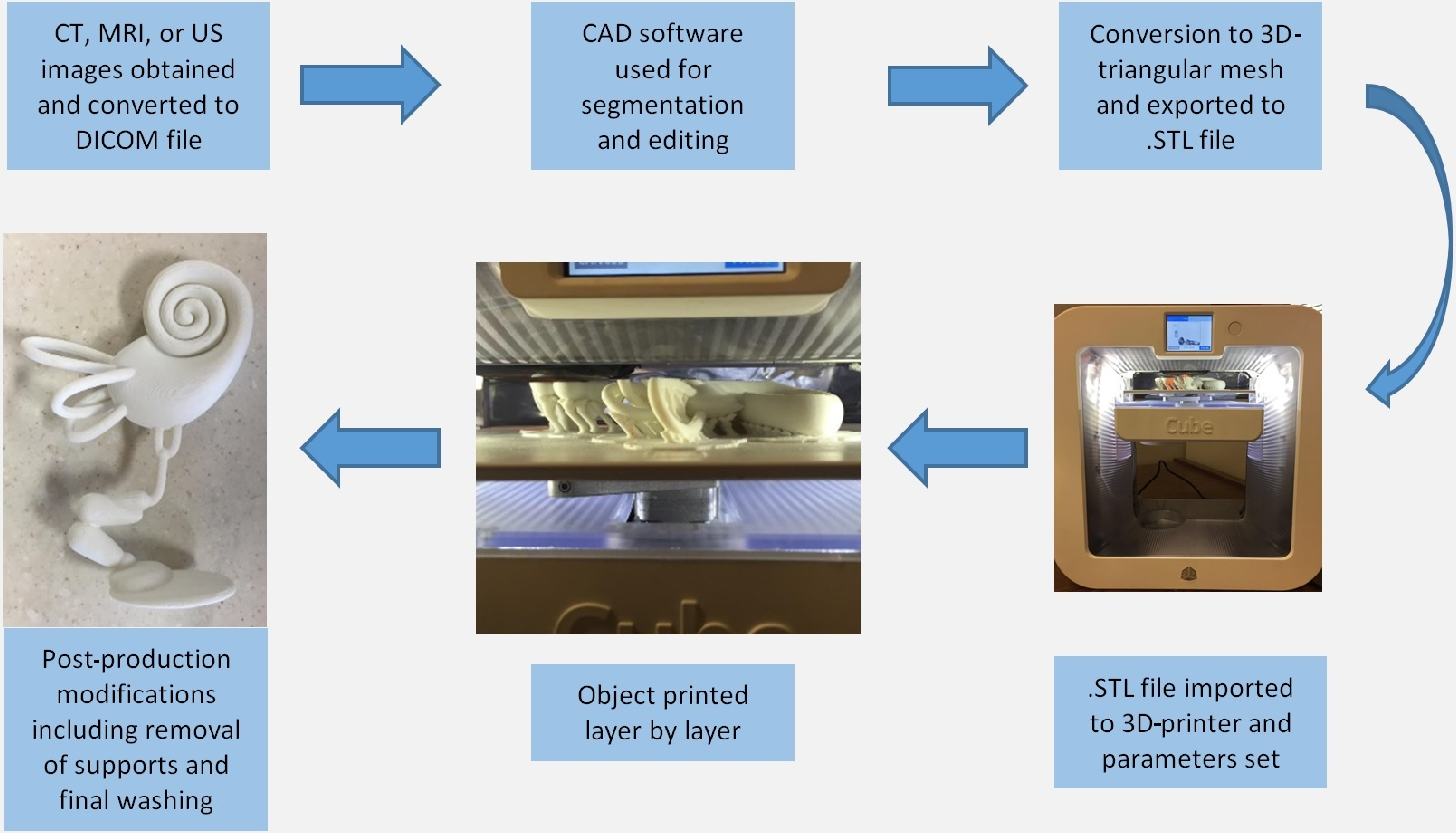

Records identified through database search (n = 1,439)
Records excluded for age > ~ 5 years (n = 241)
Records screened using title and abstract (n = 1,198)
Records excluded as showed lack of relevance to otorhinolaryngology (n = 1,157)
Records identified from additional sources including source citations (n = 28)
Records screened for additional pertinent sources (n = 41)
Records included for final review & analysis (n = 69)


CT, MRI, or US images obtained and converted to DICOM file
CAD software used for segmentation and editing
Conversion to 3D-triangular mesh and exported to .STL file
.STL file imported to 3D-printer and parameters set
Object printed layer by layer
Post-production modifications including removal of supports and final washing