Pediatric RESEARCH

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SYSTEMATIC REVIEW

Three-dimensional printing in medicine: a systematic review of pediatric applications

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BACKGROUND: Three-dimensional printing (3DP) addresses distinct clinical challenges in pediatric care including: congenital variants, compact anatomy, high procedural risk, and growth over time. We hypothesized that patient-specific applications of 3DP in pediatrics could be categorized into concise, discrete categories of use.
METHODS: Terms related to "three-dimensional printing" and "pediatrics" were searched on PubMed, Scopus, Ovid MEDLINE, Cochrane CENTRAL, and Web of Science. Initial search yielded 2122 unique articles; 139 articles characterizing 508 patients met full inclusion criteria.
RESULTS: Four categories of patient-specific 3DP applications were identified: Teaching of families and medical staff (9.3%); Developing intervention strategies (33.9%); Procedural applications, including subtypes: contour models, guides, splints, and implants (43.0%); and Material manufacturing of shaping devices or prosthetics (14.0%). Procedural comparative studies found 3DP devices to be equivalent or better than conventional methods, with less operating time and fewer complications.
CONCLUSION: Patient-specific applications of Three-Dimensional Printing in Medicine can be elegantly classified into four major categories: Teaching, Developing, Procedures, and Materials, sharing the same TDPM acronym. Understanding this schema is important because it promotes further innovation and increased implementation of these devices to improve pediatric care.

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IMPACT:

- This article classifies the pediatric applications of patient-specific three-dimensional printing.
- This is a first comprehensive review of patient-specific three-dimensional printing in both pediatric medical and surgical disciplines, incorporating previously described classification schema to create one unifying paradigm.
- Understanding these applications is important since three-dimensional printing addresses challenges that are uniquely pediatric including compact anatomy, unique congenital variants, greater procedural risk, and growth over time.
- We identified four classifications of patient-specific use: teaching, developing, procedural, and material uses.
- By classifying these applications, this review promotes understanding and incorporation of this expanding technology to improve the pediatric care.

INTRODUCTION

Pediatrics makes demands unlike any other medical specialty: clinicians must tackle compact anatomy, often with unique congenital features, and make decisions that benefit children not only in the moment but also as they grow over time. These demands require a personalized medicine approach to provide optimal care to young patients. The emerging technology of three-dimensional printing (3DP) enables this level of individualization by printing the patient's unique anatomy for patient-specific models, with applications that range from patient education to surgical intraoperative use.[1] Clinical 3DP items most commonly employ additive manufacturing, in which a digitized 3D model is manipulated and then printed in successive layers to build the desired object.[1–4] The term "additive manufacturing" is a broad category, covering more nuanced processes such as stereolithography, selective laser sintering, and fused deposition modeling which can process a wide array of materials such as metals, polymers, or even ceramics into the desired shape.[5] The result is the rapid production of high-fidelity, personalized models that can be used in complex care management.

The current literature suggests 3DP is a powerful tool that enhances clinical care; however, previous reviews were largely limited to adult care in single surgical subspecialties.[2,3,6,7] We propose that 3DP has the potential to be exceptionally valuable in the pediatric setting, as it presents elegant solutions to the challenges of caring for young patients. Tangible 3DP objects provide pediatric clinicians distinct advantages, including: facilitating communication with worried parents, assisting providers in clinical decision-making, allowing physicians to visualize complex congenital defects, and enhancing precision in complicated procedures. By analyzing and classifying patient-specific 3DP items in this new comprehensive taxonomy, we promote

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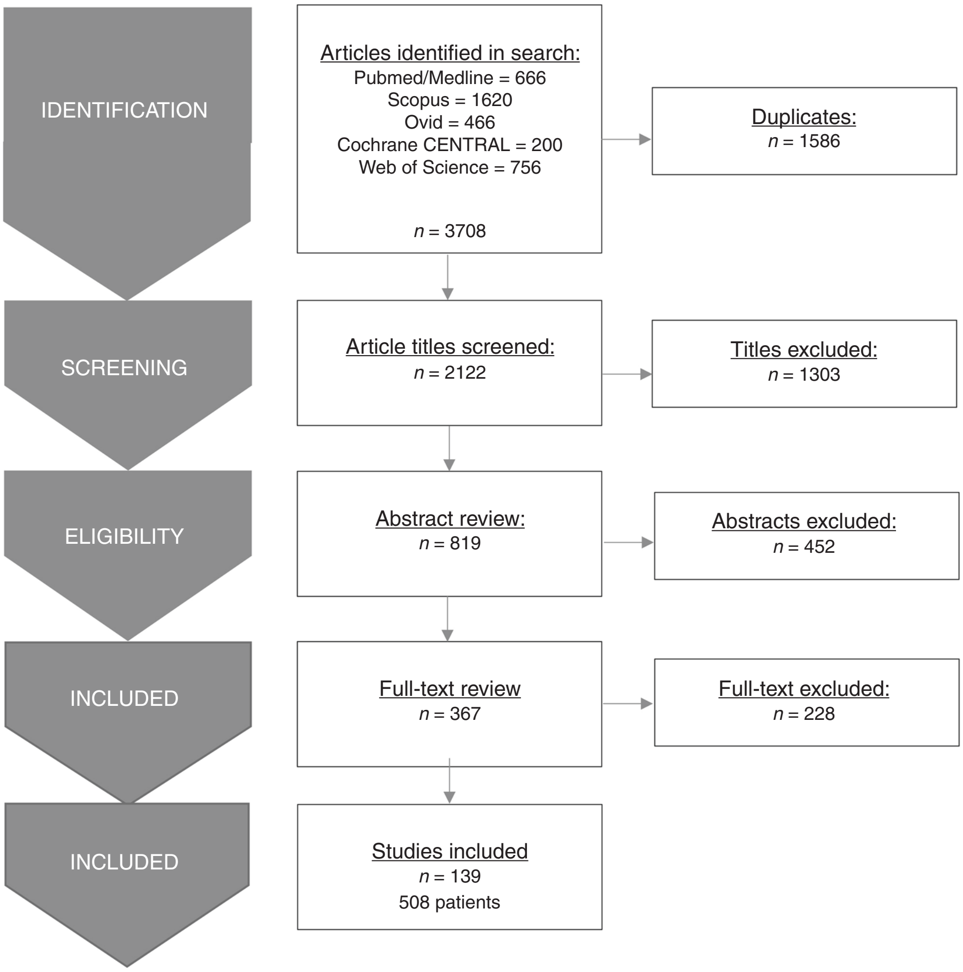

Fig. 1 Attrition flowchart. Attrition process for 139 included studies from the search of five different online databases (MEDLINE, Scopus, Ovid, CHOCHRANE Central, and Web of Science).

increased understanding and implementation of these powerful instruments of personalized medicine across the many fields of medical and surgical specialties.

This is the first systematic review of patient-specific 3DP medical applications that distinctly focuses on pediatric patients across all specialties. In this study, we categorize the way pediatric patient-specific 3DP devices are employed, compare 3DP devices against conventional methods, and identify opportunities for future integration of 3DP in the care of pediatric patients.

METHODS

Inclusion and exclusion criteria

This systematic review focuses on the pediatric applications of patient-specific three-dimensional printing (3DP) in pediatric patient-specific care. 3DP objects in this study were designed through additive manufacturing—the deposition of material in precise, successive layers to build the desired shape. Inclusion criteria required that studies: (1) manufacture 3DP objects through additive manufacturing, (2) involve the use of a patient-specific 3DP object in the clinical care of a patient either directly or indirectly, (3) report primary data, and (4) address the pediatric population, defined as patients up to and including the age of 18 years old. Studies analyzing qualitative data from adults about pediatric patients (e.g., a parent's understanding of his or her child's condition) were included as long as the patients themselves were pediatric. Both case studies and case series were included. All available publication years were considered.

Exclusion criteria were as follows: (1) reviews, technique articles, editorials, book chapters, methods papers, and incomplete articles (e.g., only abstracts available), (2) articles not available in English, (3) articles in which the 3DP object was not directly or indirectly involved in some aspect of patient care, (4) objects produced by methods other than additive manufacturing, including subtractive manufacturing, computer numerical control milling, and prototype machining, (5) studies that included patients ages 19 and older, (6) 3DP objects that were not patient-specific, meaning the same object was used in the care of multiple patients, (7) cadaver studies, (8) animal studies, and (9) tissue engineering proof-of-concept studies or tissue engineering studies conducted solely in vitro.

Systematic database search

The medical literature published in five databases (Pubmed MEDLINE, Scopus, Ovid, COCHRANE Central, and Web of Science) was searched for articles that included terms relating to "three-dimensional printing" and "pediatrics." The Medical Subject Heading terms "printing, three-dimensional," "pediatrics," "pediatric surgery," "adolescent medicine," and "infant" were included, as well as wildcard asterisked terms, to systematically review available literature.

Search results from all databases were combined, and duplicates were removed. Two reviewers independently conducted title weeds and abstract weeds for concordance of article relevance. The full-text of the relevant studies was examined for eligibility, and disagreements were discussed to reach consensus.

Data collection

Data collected from the individual articles included manufacturing variables, specialty usage, comparison data and patient-specific applications. Manufacturing data included medical imaging used to obtain data, modeling software, printers, time, and cost. Specialty was defined as the medical specialty of the senior author. Patient-specific applications were classified into broad categories of application. If the application was surgical, the type of operation was noted. Lastly, studies were searched for any comparison data that could suggest use of 3DP objects equal or superior to conventional methods.

RESULTS

The multiple database search was completed on January 11, 2018, with results combined and duplicates removed. The search delivered 2122 unique articles, and a title weed eliminated 1303 articles based on inclusion and exclusion criteria. An abstract weed was conducted on the 819 remaining articles (Cohen's kappa $k = 0.968$), and a full-text weed reviewed the resulting 367 articles ($k = 0.949$). In total, 139 articles met all criteria and were eligible for inclusion in systematic review. The attrition flowchart detailing study selection is shown in Fig. 1.

These papers contained a total of 508 patients, with an average of 3.6 patients included per study. Mean patient age was 7.6 years old. Of the 139 full-text articles reviewed, 8 were Level II, 8 were Level III, 37 were Level IV, and 86 were Level V evidence, using guidelines for therapeutic studies.[8] Manufacturing variables, specialty usage, comparison of 3DP vs. conventional methods, and patient-specific clinical applications were all examined and synthesized into a new classification schema of three-dimensional printing (3DP) use.

Manufacturing variables

Three-dimensional printing begins with the acquisition of patient data. Most commonly, these data were generated through computed tomography (CT) imaging (62.8% of all patients), but a fraction of patients did not have any medical imaging (3.4%) and instead had direct measurements (e.g., hand measurements of the contralateral side for hand prosthetics). Next, patient data were converted into a 3D digital rendering. These models could be either *positive-space models* mimicking actual patient anatomy or *negative-space models* representing the space surrounding the patient anatomy. Modeling could also be used to manipulate images into virtual positions (i.e., existing digitally only). One commonly employed manipulation was mirroring, where an ipsilateral defect is modeled with the contralateral normal side virtually reversed, to provide the ideal template.[9–15] Consequently, 3DP devices could either be positive or negative-space models of actual or virtual patient anatomy. Modeling data were then converted to printable data. A wide variety of software was used across studies, with over 25 unique software company platforms reported. Materialise (Leuven, Belgium) was the most common (19.7%). Studies also demonstrated diversity in printer selection, utilizing 20 unique printers with Stratasys (Eden Prairie, MN) as the most frequent (13.4%).

Additional factors compared across 3DP objects included time and cost. Seventy-four patients[10,16–29] (14.6%) had information available regarding production time, ranging from 0.42 to 108 hours (average 14.4 hours). Sixty-nine patients[16,26,30–36] (13.6%) had the cost of 3DP devices listed ranging from $20.75 to $4043 (average cost $895.80). Manufacturing variables are further outlined in Table 1.

Table 1. Manufacturing variables.

Variable	Percent of patients
Imaging	
Computer tomography/computer tomography angiography	63
Three-dimensional photographic scanner	13
Magnetic resonance imaging/magnetic resonance angiography	9.0
Anthropomorphic data	3.7
X-ray	1.0
Multiple modalities	7.7
No data	3.0
Modeling software	
Materialise, Leuven, Belgium	20
Slic3r (open-source software)	4.5
Blender Foundation, Amsterdam, Netherlands	3.9
Synopsys (Mountain View, CA)	3.9
3D Systems, Rock Hill, South Carolina	3.5
Autodesk Inc., San Rafael, California	3.3
Inus Technology, Inc, Seoul, South Korea	3.3
Biomedical Imaging	2.0
Meshlab	1.4
Other	4.7
Multiple platforms	22.6
No data	27
Printer	
Stratasys, Eden Prarie, MN	13
3D Systems, Rock Hill, SC	12
Fuxiang Technology, Shenzhen, China	2.2
Ultimaker, Geldermalsen, Netherlands	2.2
Edison, Rokit, Korea	1.4
Aleph Objects, Loveland, CA	1.0
Electro Optical Systems (EOS), Munich, Germany	1.0
Printrbot, Lincoln, CA	0.8
FELIXprinters, IJsselstein, Netherlands	0.8
Zortrax, Olsztyn, Poland	0.8
Dentaurum, Inspringen, Germany	0.6
Formlabs, Somerville, MA	0.6
Other	1.8
Multiple printers	3.1
No data	59
Time	
Patients with production time information	15
Average (h)	14.4
Range (h)	0.42–108
Cost	
Patients with cost information	14
Average	$895.80
Range	$20.75−$4043

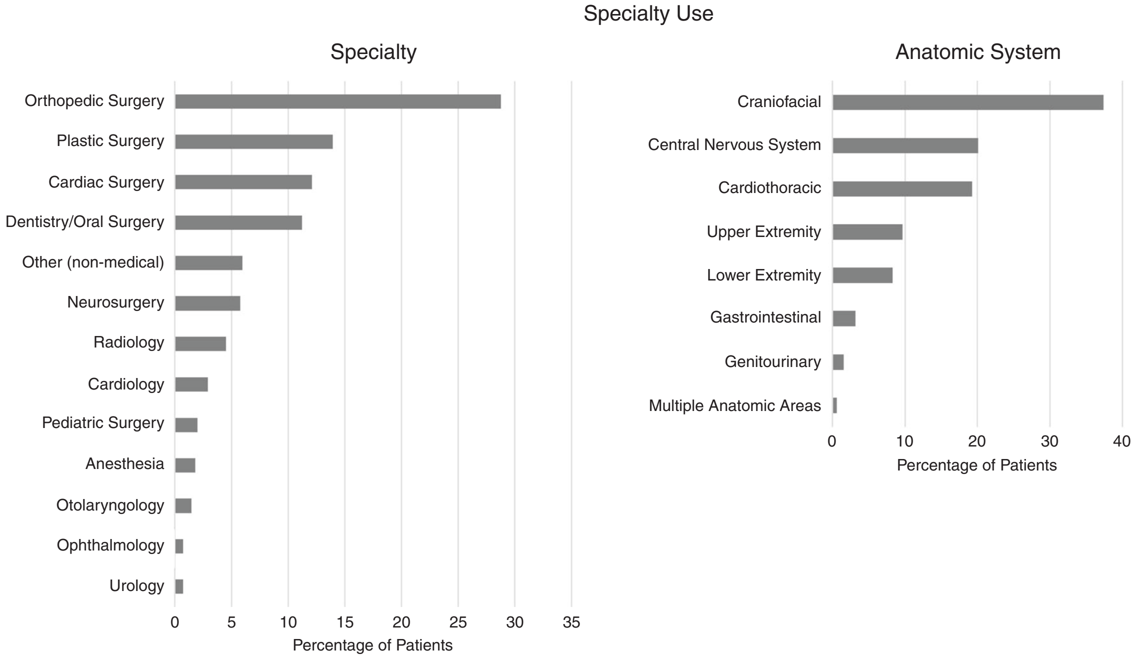

Fig. 2 Specialty use. Proportion of patient-specific applications by specialty use as determined by either the department of the last author or by anatomic areas.

Specialty use

By specialty analysis, Orthopedic Surgery had the highest volume of patients (28.8%), followed by Plastic Surgery (13.9%). When evaluating how these specialties employed 3DP items, many uses were interdisciplinary. For example, 3DP cutting guides for spinal surgery were employed by both orthopedic and neurosurgeons. To account for this interdisciplinary overlap, specialty use was also tabulated by anatomic area. Anatomic areas included: craniofacial (skull, face, jaws),[9–15,23,31–33,35,37–92] central nervous system (brain, spine),[34,93–100] cardiothoracic (heart, lungs, chest),[24–28,36,93,94,101–121] upper extremity,[16,17,19,21,22,29,30,122–127] lower extremity,[128–136] gastrointestinal (abdomen and its viscera),[18,137–139] and genitourinary,[140–142] with distributions listed in Fig. 2. Craniofacial was the highest anatomic area that employed 3DP (37.1%), with the majority of contributions from the specialty of Plastic Surgery.

Comparison studies

Only a handful of articles were pediatric comparative studies that compared 3DP models with conventional methods ($n = 6$). These six comparison studies[32,94,96,121,128,129] focused primarily on procedural applications. Findings generally indicated incorporation of 3DP devices to be equivalent to or better than conventional methods, with shorter operating times, shorter fluoroscopy exposure, more accurate hardware placement, and fewer complications.

Classification

We identified four major classifications of patient-specific 3DP applications in pediatric patients: 1. Teaching, 2. Developing, 3. Procedures, and 4. Materials, each with subtypes as listed in Fig. 3.

Class 1. Teaching classification (9.3% of all patients) most often conveyed a disease process or treatment plan to patients and their families[27,33,34,101,102,121,134,140,142,143] (6.0% all patients), but were also employed in an inter-professional setting to communicate between healthcare professionals[26,102,121] (3.3% of all patients). In one common example,[27,101,102,121] 3DP teaching models allowed parents to directly visualize their child's congenital heart disease, facilitating discussion about their child's condition. Beyond patient education, 3DP devices can be used to teach the entire clinical team; in one example of clinician education, patient-specific cardiac models were shared when transitioning care from surgeons to ICU nurses postoperatively, which empowered nurses to tailor patient care in each unique case.[26] Cardiothoracic applications were most common, comprising 81.4% of all teaching applications.

Class 2. Developing classification (33.8%) helped clinicians with two important functions: (1) determining the appropriateness of a specific diagnosis or intervention[9,17,24,27,28,33,35,36,40,54,57,59,66,71,74,76,90,98,99,103,104,106–108,111,112,117,119,120,123,126,134,137,139,142–145] (termed *Decision*, 15.7% of all patients), or (2) practicing a given procedure on a patient-specific replica[20,25,41,46,51,58,73,78,85,91,93,97,105,113,114,116,128,131,138,141] (termed *Simulation*, 18.1% of all patients), both for surgical operations and other procedures such as cardiac catheterizations. At times, decision models revealed that a procedure was unnecessary or unlikely to improve a patient's condition. In one example, a 3DP model of a complex ventricular septal defect, initially imaged with echocardiogram and CT, allowed the clinician better visualization of the defect and driving the decision not to operate and sparing the child considerable morbidity.[111] Simulation models also aimed to reduce morbidity by increasing precision of complex surgeries; for example, 3DP was used to accurately simulate a laparoscopic adrenalectomy for neuroblastoma complete with 3DP renderings of the tumor, the surrounding anatomy and even the outer abdominal cavity.[141] Developing applications were used most commonly for central nervous system applications, particularly in planning for spinal surgery (30.3% of all patients).

Class 3. Procedures classification refers to 3DP objects used intraoperatively to facilitate procedures (42.9%); it was further subdivided into four subtypes: contour model, guides, splints, and implants. *Type I—Contour* models[10,11,13,14,20,29,32,34,46,48,52,53,60–62,64,67,68,72,82,84,86,89,96,109,110,118,122,125,135,136] (10.8%) are positive-space models based on either real or virtually modeled anatomy, such as a virtually mirrored contralateral ear, printed and used as a reference to reconstruct a congenitally absent ear.[13] *Type II—Guides*[18,29,30,37,43–45,70,77,80,81,94,95,122,128,129,132,136] (24.6%) are

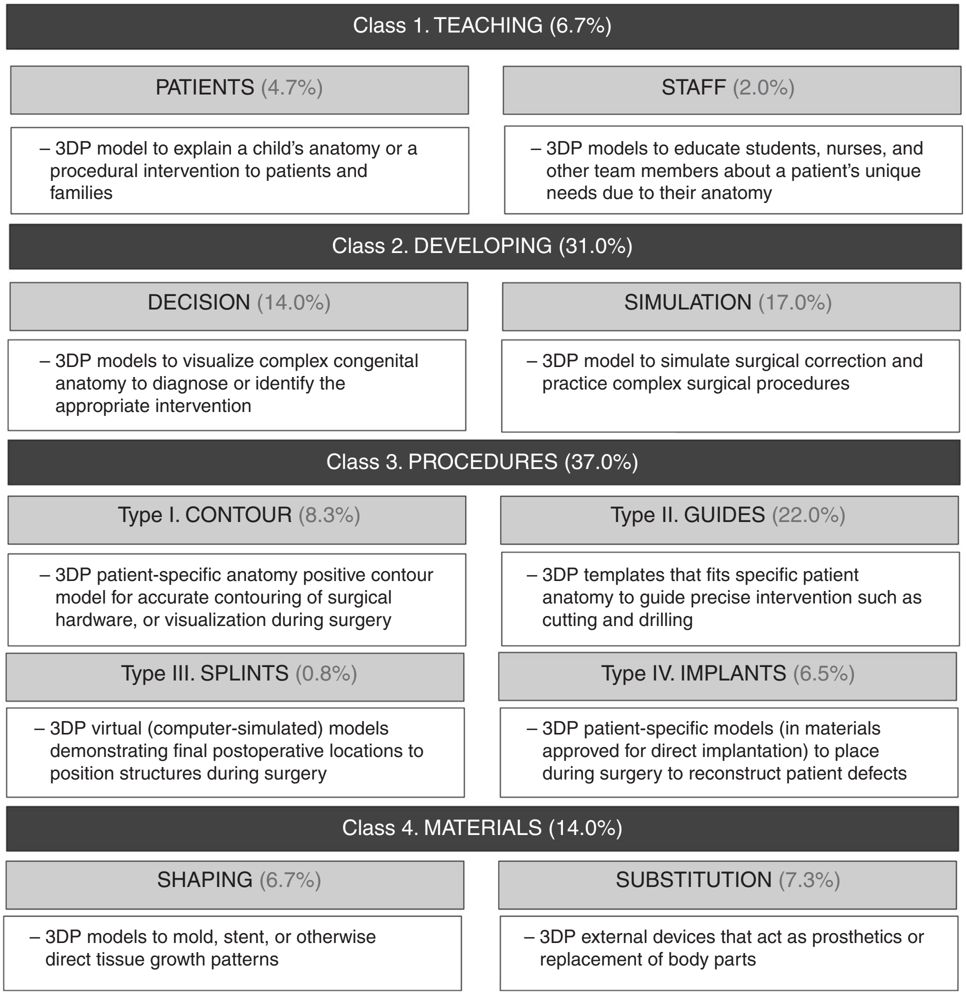

Fig. 3 The four classes of Three-Dimensional Printing in Medicine. The figure describes the four major classes of patient-specific 3DP applications: Teaching, Developing, Procedures, Materials, and their subtypes, including relative proportion of each (% represents percentage of all patients reviewed).

negative-space models based on actual patient anatomy, designed to contour to a segment of anatomy and allow for precise cutting or drilling that avoids critical structures, enabling precise screw placement in spinal surgery, for example.[34,94,95] *Type III—Splints*[31,65,73,75] (0.9%) are similar to guides in that they were negative-space 3DP items; however, unlike guides, splints were not based on preoperative anatomy but on virtual final simulated postoperative positions that were designed by virtual surgical planning. They are often used to hold anatomy in an interim position. In one example, a patient with coronal synostosis underwent reconstructive surgery to advance her frontal bone; the frontal bone was split in pieces, repositioned, and splints were used to hold the bone in ideal position before joining the fragments together with plates and screws.[31] Finally, *Type IV—Implants*[9,15,23,39,55,56,63,69,79,83,100,115,133,146–148] (6.6%) are either positive-space 3DP implantable materials or negative-space 3DP molds into which nonprintable materials are poured. Examples include thoracic vertebrae implants used to reconstruct the spine in a child with a primary bone tumor.[147] Half of all operative uses (50%) were in craniofacial applications.

Class 4. Materials classification refers to external materials that can be removed or changed (14.0% of all patients), via *Shaping*[12,38,42,47,49,88] (6.7%) and *Substitution*[16,19,21,22,124,127,130] (7.3%). Shaping devices mold patient anatomy over time, taking advantage of pediatric growth to influence results. For children with orofacial clefts, presurgical 3DP devices narrowed the gap between alveolar segments and reshaped the nostril, potentially improving symmetry and potentially reducing later secondary revisions.[38,42,47] Substitution items are external devices that replace normal anatomy (i.e., a prosthesis). 3DP prosthetic substitution objects can be rapidly printed at a relatively low cost that facilitates the frequent replacement in a growing child, allowing sequential substitution items to "grow" with a child, such as providing serial hand prosthetics that are size appropriate.[16,19,21,22,124,127] In contrast to implants, these items are removable and do not require an operation to place or remove. These items were used most commonly in Craniofacial Surgery (50.7%), typically used as shaping devices in the care of children with orofacial clefts.

Comparison studies

Only a handful of articles were pediatric comparative studies that compared 3DP models with conventional methods ($n = 6$). These six comparison studies, summarized in Table 2, focused primarily on procedural applications. Findings generally indicated incorporation of 3DP devices to be equivalent to or better than conventional methods, with shorter operating times, less fluoroscopy exposure, more accurate hardware placement, and fewer complications.

Table 2. Comparison studies.

Study	Category of use	Specialty (anatomic)	Study goal	Subjects	Outcomes
Biglino et al.[121]	Teaching	Cardiothoracic	Evaluate how 3DP heart models enhance parent understanding during cardiology consults	97 parents (45 with 3DP heart in consultation, 52 without)	– Found useful by parents and cardiologists – Parental knowledge did not improve in the 3DP group – 3DP consults averaged 5 min longer than non-3DP consults
Zheng et al.[128]	Developing, procedures	Central nervous system	Compare conventional techniques vs. 3DP guides in shortening osteotomies	25 patients (12 with 3DP guides, 13 without)	– Shorter operative times with 3DP (21.08 vs. 46.92 min) – Decreased X-ray exposure (3.92 vs. 6.69) – Decreased femoral epiphysis damage (0 vs. 0.92)
Pan et al.[94]	Procedures	Central nervous system	Compare 3DP guides vs. free-hand technique for screw placement in scoliosis correction surgery	37 patients (20 with 3DP guides, 17 free-hand)	– Operative times similar (283 vs. 285 min, $p = 0.89$) – Screw placement accuracy higher with 3DP (96.7% vs. 86.9%, $p = 0.000$)
Zheng et al.[129]	Procedures	Central nervous system	Compare 3DP surgical guides vs. conventional techniques for hip plate placement	24 patients (11 with 3DP guides, 13 without)	– Faster screw insertion time (26.50 vs. 57.15 min, $p < 0.05$) – Less intraoperative X-ray exposure (6 vs. 11.85 min, $p < 0.05$) – Less epiphyseal injury (0 vs. 3.29 times, $p < 0.05$)
Rogers-Vizena et al.[32]	Procedures	Craniomaxillofacial	Compare the cost and complication rate of midface distraction with and without 3DP for reference and pre-bending plates	29 patients (9 with 3DP models, 20 without)	– More complications in conventional group (0 vs. 7, no p value listed) – Faster operative time with 3DP models (31.3 min less per case, $p = 0.2$) – Estimated cost savings of $1036 for operative time expenses (not including model price)
Karlin et al.[96]	Procedures	Central nervous system	Compare surgical efficiency and degree of correction of spinal deformity from myelomeningocele using intraoperative 3DP reference model	17 (7 with 3DP spinal models, 10 without)	– Less fluoroscopy (0.2 min, range 0.1–0.3 vs. 0.42, range 0.3–0.6). – Less blood loss (24% blood volume, range 17–38% vs. 26%, range 13–43%) – Greater degree of spinal deformity correction (scoliosis 83% vs. 70%, kyphosis 88% vs. 76%)

DISCUSSION

The body of literature on three-dimensional printing (3DP) is rapidly expanding: of the past decade of articles available on PubMed, one-third were published in the last year of this systematic review alone. Despite this growing knowledge, previous systematic reviews have usually been more focused on adult patients, and limited to subspecialties such as Plastic Surgery,[1] Orthopedic Surgery,[7] and Otolaryngology.[6] This study uniquely includes medical and surgical applications in all specialties, focused on pediatric patients, a specialized population with unique problems that can benefit from this technology.

We were surprised to discover that with this broad range of patient-specific 3DP clinical applications, representing a wide array of medical specialties and anatomic regions, could be elegantly classified into four main classes: Class 1. *Teaching* to clarify the disease (for *Patients* and their families, or the medical *Staff*), Class 2. *Developing* a diagnosis or plan (*Decision* of diagnosis or intervention, or *Simulation* of procedure), Class 3. *Procedures* utilizing patient-specific 3DP models (*Contour* models to represent positive anatomy, *Guides* to avoid critical structures, *Splints* to set final virtual simulated positions, *Implants* to replace anatomy), and Class 4. *Materials* (*Shaping* devices to mold growing anatomy, or *Substitution* prosthetics to replace growing anatomy) (see Fig. 3). This useful classification scheme can be easily remembered, as the acronym for our taxonomy (*TDPM*: Teaching, Developing, Procedures, Materials) is the same as that for *T*hree-*D*imensional *P*rinting in *M*edicine.

Consistent with previous reviews, we found that the majority of literature was generated by surgeons. This may be explained by 3DP's ability to create high-fidelity anatomic models, which naturally benefits surgeons grappling to understand compact, complex, high-risk pediatric anatomy. In the procedures setting, 3DP was used most commonly in the care of patients with craniofacial deformities (skull, jaws, face). This is consistent with previous reviews of surgical literature, which describe Craniofacial Surgery as the most prevalent surgical application of 3DP.

Our proposed taxonomy broadly covers surgical and nonsurgical, incorporating the largest number of pediatric patients to date. Previous surgical reviews[2] of 3DP devices subcategorized studies as anatomic models, surgical instruments, or prosthetics, a system that lacks the granularity of our classification. For example, it does not differentiate between surgical guides and splints, which have distinctly different computing requirements to generate virtual anatomy for the latter. Other medical reviews of 3DP devices[149] have also highlighted some categories included in our system such as preoperative planning and patient–doctor communication, but did not account for the complexity of intraoperative uses detailed in this study. Furthermore, our study incorporates previously existing work: Our Class 3 Procedures found the same subtyping of contour, guides, splints, and implants, consistent with what was first described by Jacobs and Lin[1] in their review of craniomaxillofacial surgery, showing that their categorization remains robust for our pediatric-only systematic review. Therefore, our new taxonomy integrates previous studies and builds upon

Table 3. Patient-specific clinical utilization of 3DP by anatomic system.

- Craniofacial
  - Airway support[23,63,113]
  - Cranioplasty/cranial vault remodeling[31,39,40,54,56,83,84,89]
  - Dentistry/oral surgery[33,48,60–62,64,68,70,72,77,81,85]
  - Distraction osteogenesis[32,37,41,43,44,51,59,65,73,91]
  - Ex-utero intrapartum treatment of craniofacial abnormalities[57]
  - Microtia repair/prosthesis[9,11,13–15]
  - Nasal alveolar molding/orthodontics[12,38,42,47,49]
  - Orbital reconstruction[53,86,88]
  - Orthognathic surgery[75]
  - Repair of skull base defect[35,58,67,90]
- Central nervous system
  - Cervical spinal fusion[98]
  - Meningomyelocele[96,99]
  - Scoliosis[34,93–95]
  - Tumor resection[97,100,143,146,147]
- Cardiothoracic
  - Coarctation of aorta[25,118]
  - Double outlet right ventricle[24,105–107,112,119,120]
  - Heart transplant[109]
  - Other congenital heart disease[26,101–103,108,117,121,144]
  - Other vascular anomalies[24,107,110,116,139]
  - Pulmonary atresia[104,107]
  - Transposition of the great arteries[27,36,107]
  - Truncus arteriosus[27]
  - Ventricular septal defect[105,106,110,111,114,119,120]
- Upper extremity
  - Hand transplant[123,126]
  - Prosthetic hands[16,19,21,22,123,124,127]
  - Tumor resection[17]
- Lower extremity
  - Clubfoot[130]
  - Developmental hip dysplasia[128,129,134]
  - Limb lengthening[135]
  - Slipped capital femoral epiphysis[131]
  - Corrective osteotomies[29,30,125]
- Gastrointestinal
  - Adrenalectomy[141]
  - Liver transplant[138]
  - Hepatectomy[18]
  - Tumor resection[20,137,141,142]
- Genitourinary
  - Cloacal malformation[140]
  - Tumor resection[20]

them to create a comprehensive characterization of 3DP across the field of pediatric medicine.

Although over two-thirds of patients had surgical applications of 3DP, this study highlights the breadth of 3DP across all pediatric disciplines. No single field or single procedure dominated, with over 40 unique conditions described by the articles reviewed (Table 3). Manufacturing variables reflected similar diversity, with over 25 software platforms and 20 different printers used in the articles included in this review. The broad range indicates that universal production standards are not yet in place.

As with all systematic reviews, this study is limited by the papers and data available, subject to publication bias. Some papers did not provide information on variables we collected (e.g., time, cost, etc.) which may paint an incomplete picture of associated manufacturing variables. The caliber of the compiled studies also limits this review: most studies were retrospective case series, and only six were comparative studies that all showed 3DP devices are better or equivalent to conventional methods (Table 3). Although overall our pediatric systematic review suggests that 3DP models improve care, more case-matched comparative studies are needed. Herein lies the difficulty of analyzing 3DP: the most complex anatomy or rare congenital cases that can especially benefit from 3DP are exactly the unique type of cases that are less likely to have a comparison group.

The breadth of 3DP application uncovered in this systematic review suggests clinicians are just scratching the surface, with significant potential for future patient-specific pediatric applications. One area for expansion is the integration of new imaging modalities. Seventy percent of studies employed computed tomography (CT) to create 3DP devices. Generating 3DP items from other imaging modalities including MRI, ultrasound, and 3D-photography could limit the morbidity of ionizing radiation in children, expanding the utility of 3DP in pediatrics. In addition, close examination of our taxonomy points to areas of further potential growth. Class 4. Materials, especially *Shaping* devices, offer a unique potential to mold a child's changing anatomy to potentially avoid morbid surgeries. Unlike their adult counterparts, children have malleable anatomy that allows for molding forces of external materials to influence growth patterns. One prime example is the use of 3DP devices to premold orofacial clefts before surgery to potentially improving outcomes and sparing children from secondary revisions. This hints at the importance of this new category—by harnessing materials to influence growing pediatric anatomy, clinicians could potentially reduce the severity of surgery or avoid surgery all together. This newly identified application is relatively untapped with only six studies found in this systematic review, warranting expanded exploration of this application's potential.

This study investigates the patient-specific uses of 3DP in pediatric populations and identifies a new taxonomy of use. This taxonomy illustrates the diversity of 3DP applications and challenges clinicians to integrate it into their own practice to provide individualized approaches to their patients' problems. Furthermore, this study shows there is little standardization of these objects across disciplines. With this rapid expansion of 3DP, and the exciting potential for advanced manufacturing techniques, there is a need for a structured, regulated production process to ensure the safety and credibility of 3DP objects. Standardization may also allow for more streamlined and easily accessible production, further empowering clinicians to become actively involved in the process of 3DP patient-specific models and innovating further applications in treating pediatric patients.

CONCLUSION

Three-dimensional printing (3DP) is transforming medicine with customized patient-specific models that are especially applicable for pediatric patients with smaller anatomy, unusual congenital and acquired defects, and less room for error. Our systematic review uniquely focused on patient-specific 3DP applications in this special population, and we identified a new taxonomy with four distinct, comprehensive classes of Three-Dimensional Printing in Medicine: Teaching, Developing, Procedures, Materials. These applications of 3DP are particularly advantageous in pediatric medicine, as patient-specific 3DP models educate patients and families; expose underlying anatomy in complex congenital cases to help develop clinical plans; improve procedural accuracy, safety, and efficiency; and create rapid, cost-effective materials that accommodate a growing child. This taxonomy helps categorize what is currently available, helping to promote further innovation and support incorporation of this individualized, patient-centered care into the field of pediatrics.

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AUTHOR CONTRIBUTIONS

C.A.F. and A.M.S. designed the study, coordinated data collection, acquired data, carried out the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript. W.T.K. conceptualized and designed the study, analyzed and interpreted data, and critically reviewed and revised the manuscript for important intellectual content. A.Y.L. conceptualized and designed the study, supervised data collection, analyzed and interpreted data, and critically reviewed and revised the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

ADDITIONAL INFORMATION

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