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Effectiveness of 3D-printed models prepared from radiological data for anatomy education: A meta-analysis and trial sequential analysis of 22 randomized, controlled, crossover trials

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Abstract:

BACKGROUND: Many academicians suggested the supplementary use of 3D-printed models reconstructed from radiological images for optimal anatomy education. 3D-printed model is newer technology available to us. The purpose of this systematic review was to capture the usefulness or effectiveness of this newer technology in anatomy education.

MATERIALS AND METHODS: Twenty-two studies met the inclusion and exclusion criteria for quantitative synthesis. The included studies were sub-grouped according to the interventions and participants. No restrictions were applied based on geographical location, language and publication years. Randomized, controlled trial, cross-sectional and cross-over designs were included. The effect size of each intervention in both participants was computed as a standardized mean difference (SMD).

RESULTS: Twenty-two randomized, controlled trials were included for quantitative estimation of effect size of knowledge acquisition as standardized mean difference in 1435 participants. The pooled effect size for 3D-printed model was 0.77 (0.45–1.09, 95% CI, $P < 0.0001$) with 86% heterogeneity. The accuracy score was measured in only three studies and estimated effect size was 2.81 (1.08–4.54, 95% CI, $P = 0.001$) with 92% heterogeneity. The satisfaction score was examined by questionnaire in 6 studies. The estimated effect size was 2.00 (0.69–3.32, 95% CI, $P = 0.003$) with significant heterogeneity.

CONCLUSION: The participants exposed to the 3D-printed model performed better than participants who used traditional methodologies. Thus, the 3D-printed model is a potential tool for anatomy education.

Keywords:

Cognition, goals, immersion, motivation, printing, reaction time, spatial navigation, three-dimensional, tomography, X-Ray computed

Introduction

Anatomy is the cornerstone of medical education along with clinical practices for medical and allied health students. The acquisition of anatomical knowledge is mainly concerned with identifying and finding relations of any organ or structure.^[1]

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Medical students or residents need spatial orientation and visualization of human body structures for clinical teaching or practice, other than their functions. Students often find topics difficult because of complex spatial relations.^[2] Cadaveric dissection or wet cadaveric prosection is the yardstick for anatomy teaching, which is traditionally

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employed as a normal educational framework to assist students in learning anatomical structure, three-dimensional (3D) orientation, and gaining practical skills.^[3,4] A lot of money, time, and expertise are utilized during the preparation, maintenance, and disposal of cadaveric specimens. An expressive or meaningful collection of these specimens would be expensive to manage and afford for every medical school. Plastinated specimens became a popular and dependable alternative.^[5] Casting and molding-based plastic models were less realistic and were only suited for teaching elementary anatomy.^[6]

Further advancement with the availability of 3D printers made it feasible to make cost-effective, high-quality copies of human anatomical organs and body parts in a wide variety of textures and colors from 3D-reconstructed images of computerized tomography (CT) scan or magnetic resonance imaging (MRI) scan.^[7] Several researchers have experimented with this additive technology to create anatomical models using CT or MRI images.^[6,8] Anatomy teachers also have opportunities to develop 3D-printed models (3DPMs) from radiological scans of patients on case basis.^[9] It is highly customized and extraordinarily detailed, which was impossible earlier in the molded physical model. Such models have very minute details, equivalent to dissected cadaveric specimens. Their handling has improved students' visuospatial consciousness, tactile sensation, and decreased cognitive load.^[10] Students can also learn the pathological anatomy of any structure they often miss in cadaveric dissection.^[11] Many trials have been conducted in the past to assess its actual benefits among learners.

Medical students preferred novel 3DPMs as learning tools and expressed their idea and argued with their favorable comments on increasing engagements, orientation and recognition of diverse anatomical details of the structure.^[4,7,12] Additionally, they enumerated several benefits of using 3DPMs, for example, color labeling, ease of handling, less fear of damaging the structure, and fewer psychological inhibitions while engaging with the 3DPM [Figure 1]. It was difficult to grasp 3D relationships and build mental representations using static 2D pictures, as opposed to 3DPMs, which could be held in all directions and rotated.^[6-8,10]

When students were tested for anatomical knowledge between 3DPMs and standard cadaveric materials, the 3DPM group performed better than the cadaveric group.^[13-15] However, the results of the research were limited by a number of factors, such as a small sample size and a focus on relatively easy anatomical topics.^[14,16,17] Many researchers outlined the benefits and educational value of these models; however, these innovative tools had not yet been widely implemented in anatomical education.^[6,7,13] Many empirical investigations

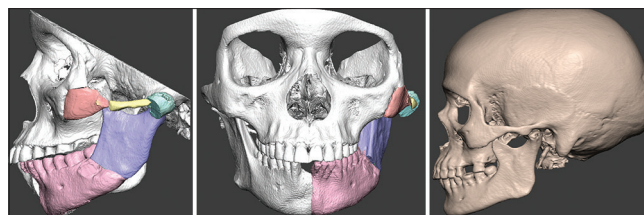


Figure 1: 3D-printed model of skull from CT data prepared at the 3D printing lab (department of anatomy). It is accurate and allows for easy handling. Multiple copies of the same model (partly or even single bone) can be prepared along with the colored region of interest

revealed the potential and superiority of 3DPMs above the traditional approach in terms of effective learning and performance. There was a need for further evidence before these approaches could be widely adopted in conventional medical education.

Stakeholders believe 3DPMs can provide a valuable contribution to anatomy education. To test our hypothesis in this context, we explored the learner's benefit based on the available data in published literatures. Could it support the idea that 3DPM is a supplementary tool in anatomy education based on the critical evaluation of published literature? The current systematic review was conducted to evaluate its effectiveness and impact on anatomy teaching comprehensively. The review also glanced at the mechanisms behind its efficacy and assimilation into modern curricula based on learning principles, as well as the attributes that drive its utility.

Materials and Methods

Study design and setting

Population: Undergraduate and residents of medical or allied health courses where anatomy is taught as a subject.

Intervention: 3DPM prepared from radiological data.

Comparator: Traditional method like textbook, atlas, PowerPoint slides and chalk-board teaching.

Outcome: Kirkpatrick's model of educational outcomes [Figure 2] is utilized as an evaluation framework for classifying and analyzing results of an educational intervention (3DPM model).^[18] In this model, postinterventional changes in learners are captured in the form of reaction (learner experience), learning (changes in attitude, knowledge, and skill), behavior (shift in practice and application of learning), and results (changes in practice or application at the level of organization). Here, we captured only the first two main outcomes:

(A) Learning (Level 2): Knowledge by changes in test score or accuracy. It also corresponds to level 1 of Miller's pyramid.^[19]



Figure 2: Kirkpatrick model of educational outcomes evaluation (Kirkpatrick 2016)

(B) Learner’s experience (Level 1): Changes in learner’s satisfaction, confidence level, utility, and engagement by test completion time.

Figure 2 shows the Kirkpatrick model of educational outcomes evaluation.^[18]

Inclusion criteria

1. Population: Students or residents of health professional courses.
2. Studies addressing the impact or effectiveness of 3DPM as an intervention in surgical and radiological anatomy along with patho-anatomy.
3. Randomized controlled trials (parallel or cross-over), prospective and retrospective observational studies were included if the 3D anatomy tool was used as an intervention.
4. The 3DPM prepared from radiological images as anatomy education tools on student or resident learning were included.
5. The radiological images used for creating 3D models should be computerized tomography (CT) scan, magnetic resonance imaging (MRI), ultrasonography, and positron emission tomography (PET) scan.
6. The comparator would be the traditional approaches, including textbooks, two-dimensional (2D) images or atlas, lecture notes, tutorial notes, 2D illustrations, PowerPoint slides, and text-focused resources.
7. The outcomes measured were (a) factual knowledge, spatial orientation measured by test score or accuracy (Kirkpatrick level 2 and Miller’s knowledge and applied frame work), (b) the reaction of participant, for example, the satisfaction score, response time, usefulness, confidence (Kirkpatrick level 1) (Kirkpatrick 2016).

8. English language manuscripts.

Exclusion criteria

1. Population: Faculty or non-academic trainee.
2. Following interventions were excluded: Physical plastic model, clay model, plaster of Paris model, plastinated model, and mounted cadaveric viscera.
3. Commercially procured 3DPM model.
4. Descriptive studies or narrative meta.
5. Studies related to planning and making 3D models.
6. 3D model studies dealing with bioengineering and developing implants.
7. Non-English language manuscript.
8. Surgical planning, diagnosis, simulation
9. Presurgical training.
10. Patient education.
11. The outcome as a preference or choice or acceptance.

Study selection

The search strategy collected relevant studies from electronic databases like ERIC, OECD, PubMed, Google Scholar, Scopus, and EMBASE. The MeSH terms and their synonyms were used to search for studies. The search strategy is mentioned here (“3D printed” OR “3D printing” OR “3D printed” OR “3-D printing” OR “3-dimensional printed” OR “3-dimensional printing” OR “three-dimensional printed” OR “three- dimensional printing”) AND “anatomy” AND (“education” OR “teaching” OR “learning”). Other sources like online anatomy and medical education journals, the hard copies of anatomy and medical or dental education journals were also searched. The searched items were transferred to Rayyan QCRI app to shortlist the studies based on inclusion and exclusion criteria. Two reviewers used the inclusion and exclusion criteria to shortlist the studies independently. The duplicated items from different search strategies were removed. The third reviewer provided input during conflicting opinions of the first two reviewers. The protocol was prospectively registered in PROSPERO (CRD42021249906).

Methodological quality assessment

This review employed the risk of bias assessment by Medical Education Research Study Quality Instrument (MERSQI).^[20] Risk of bias was assessed by observing the studies for random sequence generation and allocation concealment, blinding of investigator and participant, blinding of outcome assessment, and selective reporting. Each item was categorized into low risk, unclear, and high risk of bias. Two independent reviewers executed the risk of bias assessment.

Data extraction and analysis

The full texts of included studies were assessed for author, publication year, DOI number, country, institution, journal, type of research, participants, intervention, sample size, outcomes of the intervention, and items of

risk bias assessment of MERSQI. The extracted data were mapped for synthesizing the qualitative and quantitative shreds of evidence. The original author was contacted via email for missing data. Test score, time of completion of test, satisfaction score, and sample size of the control and intervention groups were recorded. These data recorded were expressed as mean and standard deviation or median and interquartile range. The median and interquartile range were converted to mean and standard deviation, respectively, by the appropriate formulae.

The heterogeneity statistics were measured with Cochrane Q , tau square, and i^2 statistics. If heterogeneity was more than 50%, the random effect model was used; otherwise, the fixed-effect model was used for effect size estimation. Subgroups were created to deal with heterogeneity. The effect size of each study was computed as a standardized mean difference (SMD) because of variable scale of assessment in pretest and posttest. Then SMD of each study was combined into meta-analysis by inverse variance method to get pooled effect size. Then final i^2 statistics, Cochrane Q , and Z-score were calculated. The sensitivity analysis was conducted leaving out each study, and cumulative analysis was executed by adding each study in sequence. We were not able to reduce heterogeneity during the data analysis. The cumulative alpha error ($\alpha = 0.05$) of included studies and high heterogeneity might shift the Z-curve of the pooled effect size during random effect model of meta-analysis. Trial Sequential Analysis (TSA) version 0.9 (Copenhagen Trial Unit, Denmark) was utilized to calculate pooled estimates after adjusting the threshold for statistical significance ($\alpha = 0.05$ and $\beta = 0.2$) to overcome the above errors and to estimate the required information size (RIS). TSA monitoring borders were set at a 95% confidence interval and cumulative Z-curve was evaluated sequentially after the addition of included studies.

Results

Characteristics of included studies

The search strategy resulted in 7539 items from all digital sources and 217 items from other sources. Seventeen hundred fifty-three were found to be nonduplicate items, leaving 6003 things. The titles and abstracts of items of 341 were shortlisted from 1753 items in Rayyan QCRI app, and finally keeping 106 items, the rest of the articles were excluded in the screening phase. The full texts of 106 studies were assessed, and 84 were excluded from review due to different reasons, for example, inadequate outcome or missing data, etc., [Figure 3]. A total of 22 studies were included in the review and quantitative analysis. Of the 22 studies included in the review, 10 were from Asia, 4 from Europe, and 8 from North America. None of the studies were reported from Australia, Africa, and South America [Tables 1 and 2].

Fourteen studies dealt with undergraduate students of medical, dental, and allied health sciences, whereas 8 studies dealt with residents and interns [Tables 1 and 2].^[12–17,21–36]

Effect of interventions

Factual knowledge and spatial orientation (Kirkpatrick level 2): Both outcomes were tested either by test score or accuracy in the studies.

a. Based on knowledge score: Twenty-two randomized, controlled trials studied the effectiveness of 3DPM in 1435 participants. The 3DPM group had 722 participants and 2D or tradition group had 713 participants in all trials. The pooled effect size (SMD) of 3DPM was 0.77 (0.45–1.09, 95% CI, $P < 0.0001$) with 86% heterogeneity [Figure 4]. Subgroups were created based on population and intervention.

Fourteen studies were included in the undergraduate subgroup. The estimated pooled effect size among the undergraduate students was 0.97 (0.57–1.37, 95%CI, $P < 0.001$) with 88% heterogeneity among studies. A total of 9 studies were included in the resident subgroup. The pooled effect size (knowledge score) was 0.45 (–0.07 to 0.97, 95% CI, $P = 0.09$) with 83% heterogeneity [Figure 4]. 3DPM of the musculoskeletal and nervous systems were more effective, but the same were not established for cardiac and gastro-intestinal models. The effect size for musculoskeletal intervention was 0.86 (0.50–1.22, 95%CI, $P < 0.001$) with 76% heterogeneity. For nervous system 3DPM intervention, the pooled effect size was 1.06 (0.59–1.53, 95% CI, $P < 0.001$) without any heterogeneity [Figure 5]. Subgroup group analysis did not appear fruitful in reducing the heterogeneity, and trial sequence analysis was considered for evaluation of impact of associated heterogeneity on pooled effect size (cumulative Z-curve).

In trial sequence analysis was implemented to follow the cumulative Z-curve (blue line) and heterogeneity-adjusted cumulative Z-curve (green line) to assess the impact of existing heterogeneity [Figure 6a]. Both lines ran in significant zone beyond (2SD) and indicated that the 3DPM intervention was significantly effective in undergraduate population. The estimated RIS was 734 which was already achieved. No further trial is needed to evaluate the benefits of 3DPM in anatomy education for undergraduates. For residents, cumulative Z-curve (blue line) just crossed the boundary of insignificant zone, but green line (heterogeneity adjusted Z-curve) was still within the boundary of insignificant zone as shown in Figure 6b. Thus, the pooled effect size for residents was insignificant and RIS was yet to be achieved ($n = 893$). So, further studies need to be conducted to compute final effect size.

b. Accuracy: Only two studies dealt with accuracy scores based on the corrected items. The effect size

Table 1: MERSQL tool used for quality assessment for included studies

Domains - Authors - Year [Ref.]	MERSQL														
	Design Study design	Number of institutions	Sampling rate	Response rate	Assessment	Type of data	Validity of evaluation instrument		Data analysis Complexity of analysis	Outcome Study variable	Total (18) Score	ROB	Ethnicity	Name of intervention	
						Internal structure	Content	Relationships to other variables	Appro priateness of analysis	variable outcome					
Chedid <i>et al.</i> , 2020 ^[26]	3	0.5	1	2	1	1	1	0.5	0.5	2	1.5	13	Low	North American	3D-printed model of Liver
Vidaurre <i>et al.</i> , 2019 ^[27]	1.5	0.5	0	1	0	0.5	0	0.5	0.5	1	1.5	6.5	High	European	3D-printed cardiac model
Yi <i>et al.</i> , 2019 ^[17]	3	0.5	0	1	1	1	1	1	1	1	1.5	11	Low	Asian	3D-printed model of ventricle of brain
Low <i>et al.</i> , 2019 ^[31]	3	0.5	0	1	0	1	1	0.5	1	1	1.5	9.5	Low	North American	3D-printed frontal sinus
Bangeas <i>et al.</i> , 2019 ^[23]	3	0.5	0.5	1	0	1	1	0.5	0.5	1	1.5	9.5	Low	European	3D-printed model anal canal
Cai <i>et al.</i> , 2019 ^[25]	2	0.5	0.5	1	0.5	1	1	1	1	1	1.5	10	Low	Asian	3D-printed knee
Wang <i>et al.</i> , 2020 ^[32]	3	0.5	0.5	1	1	1	1	0.5	0.5	1	1.5	10.5	Low	Asian	3D-printed cardiac model
Wu <i>et al.</i> , 2018 ^[34]	3	0.5	0.5	1	0	0.5	0	0.5	0.5	1	1	8	High	Asian	3D-printed model of wrist, ankle, pelvis and spine
Awan <i>et al.</i> , 2018 ^[22]	3	0.5	0.5	1	1	1	1	0.5	1	1	1.5	11	Low	North American	3D-printed hip
Chen <i>et al.</i> , 2020 ^[12]	3	1	0	1	0	0.5	0	0	1	1	1.5	9	Low	Asian	3D-printed gastrocolic trunk
Al-all <i>et al.</i> , 2017 ^[21]	3	1	0	1	1	1	1	0	1	1	1.5	10.5	Low	European	3D-printed lip
Hojo <i>et al.</i> , 2019 ^[29]	3	0.5	0.5	1	1	1	1	0	1	1.5	1.5	11	Low	Asian	3D-printed pelvis
Hojo <i>et al.</i> , 2019 ^[29]	3	0.5	0.5	1	1	1	1	0	1	1	1.5	10.5	Low	Asian	3D-printed pelvis
Jones and Seckeler, 2017 ^[28]	3	0.5	0.5	1	0.5	1	1	0	1	1	1.5	10	Low	North American	3D-printed aorta
Bohl <i>et al.</i> , 2019 ^[24]	3	0.5	0.5	1	0	1	1	0	1	1	1.5	9.5	Low	North American	3D-printed lumbar spine (CT)
Su <i>et al.</i> , 2018 ^[36]	3	0.5	0.5	1	1	1	1	0.5	1	1	1.5	11	Low	Asian	3D-printed heart model
Chen <i>et al.</i> , 2017 ^[13]	3	0.5	0.5	1	1	1	1	0.5	1	1	1.5	11	Low	Asian	3D-printed skull
Smith <i>et al.</i> , 2017 ^[14]	3	0.5	0.5	1	0	1	1	0.5	1	1	1.5	10	Low	European	3D-printed bones and lungs

Contd...

Table 1: Contd...

Domains - Authors - Year [Ref.]	Design Study design	Sampling		Type of data		Validity of evaluation instrument		Data analysis		Outcome Study variable outcome	Total (18) Score	ROB	Ethnicity	Name of intervention	
		Number of institutions	Response rate	Assessment	Internal structure	Content	Relationships to other variables	Appro priateness of analysis	Complexity of analysis						Study variable outcome
White <i>et al.</i> , 2018 ^[33]	2.5	0.5	0	1	1	1	0.5	0.5	1	1.5	9.5	Low	North American	3D-printed heart	
White <i>et al.</i> , 2018 ^[33]	2.5	0.5	0	1	1	1	0.5	0.5	1	1.5	9.5	Low	North American	3D-printed heart	
Li <i>et al.</i> , 2015 ^[16]	3	0.5	0	1	1	1	0.5	1	1	1.5	10.5	Low	Asian	3D-printed spine	
Lin <i>et al.</i> , 2018 ^[35]	3	0.5	0	1	1	1	0.5	1	1	1.5	10.5	Low	Asian	3D-printed skull base	
Tanner <i>et al.</i> , 2020 ^[15]	2.5	0.5	0.5	2	1	1	1	1	1.5	2	13	Low	North American	3D-printed skull (Pterygopalatine fossa)	
Tanner <i>et al.</i> , 2020 ^[15]	2.5	0.5	0.5	2	1	1	1	1	1.5	2	13	Low	North American	3D-printed skull (Pterygopalatine fossa)	
Loke <i>et al.</i> , 2017 ^[30]	3	0.5	0.5	1	1	1	0.5	1	1	1.5	11	Low	North American	3D-printed cardiac model	

estimated for the 3DPM (represented as SMD) was found to be 2.81 (1.08–4.54, 95% CI, $P = 0.001$) with 92% heterogeneity [Figure 7]. Both blue and green lines ran in the significant zone in TSA. Thus, it played a significant role in improving the accuracy of the test.

Student’s or resident’s reaction (Kirkpatrick level 1)

a. Satisfaction

The satisfaction score was examined through questionnaires for 245 participants of 6 studies. The estimated effect size was 2.00 (0.69–3.32, 95% CI, $P = 0.0001$) with significant heterogeneity [Figure 8]. The heterogeneity statistics (i^2) was 95%. In the trial sequence analysis, both Z-curve line were in significant zone and the sample size had crossed RIS ($n = 393$). It led to higher satisfaction score in participants.

b. Test completion time

The response time or time to complete the test was studied in 474 participants of 3 studies. The 3DPM group had 237 participants and 2D or tradition group had 237 participants. The effect size (SMD) was computed via random effect model which was found to be - 0.88 (-1.94 to 0.17, 95% CI, $P = 0.1$) with significant heterogeneity ($i^2 = 94%$) [Figure 9], and the meta-analyzed measure of effect was found to lie on the no effect line. Hence, we observed that 3DPM intervention did not reduce test completion time. TSA evaluation showed a similar result and calculated RIS was not achieved ($n = 6447$). Thus, it did not reduce the test completion time for participants.

c. Utility

Two studies examined the utility of 3DPM tools. A total of 120 participants were rated for both 3DPM and 2D or traditional method. The effect size was calculated by adopting the random effect model and the estimated benefit ratio was 1.97 (0.83, 4.64, 95% CI, $P = 0.12$) with 82% heterogeneity [Figure 10]. Participants did not find it as a significantly better utility tool than the traditional model.

d. Confidence Level

The confidence level was reported by only 4 studies. The effect size of the confidence level was computed as SMD, which was 0.48 (-0.27 to 1.23, 95% CI, $P = 0.21$) [Figure 11]. No significant difference of confidence level was observed in participants of the 3DPM group over the traditional group. TSA result had similar findings but RIS was not achieved.

Publication bias

On examination of the funnel plot of the primary outcome, authors have found no publication bias. All

Table 2: The characteristics of included studies in systematic review and meta-analysis

Authors - year	Name of intervention	Total	Mean age with SD	Primary outcome	Secondary outcome	Name of intervention	Total	Primary outcome	Secondary outcome
Chedid <i>et al.</i> , 2020 ^[26]	3D-printed model of liver	58 residents	32.7 (8.2)	Pretest score: 42 (33); Post test score: 77 (19)	Confidence (2.8); Posttest: 6.6 (2.2)	2D Image of liver	58 residents	Pretest score: 39 (31); Posttest score: 69 (20)	Confidence Pretest: 4.1 (2.9); Posttest: 6.2 (1.8)
Vidaurre <i>et al.</i> , 2019 ^[27]	3D-printed cardiac model of left ventricle outflow obstruction	118 students	NA	Pretest score: 8.32/14; Posttest score: 12.60/14	Satisfaction	Lecture	118 students	Pretest score: 8.35/14; posttest score: 11.20/14	Satisfaction
Yi <i>et al.</i> , 2019 ^[17]	3D-printed model of ventricle of brain	20 students	19 (19-20)	Change of score: 54.38 (10.53)	Confidence: 3.5 (0.95); Satisfaction: 4.6 (0.55)	2D Image	20 students	Change of score 45.21 (8.38)	Confidence 2.3 (1.17) satisfaction 3 (0.7)
Low <i>et al.</i> , 2019 ^[91]	3D-printed frontal sinus	21 residents	NA	Change of test score: 3.3 (1.8)	Confidence: 23.5 (15.1)	2D illustration of frontal sinus	19 residents	Knowledge change of score 3.2 (1.8)	% Confidence 28.6 (12.7)
Bangeas <i>et al.</i> , 2019 ^[23]	3D-printing model anal canal (Fistula)	10 resident	NA	Test score: 87.2 (82.6-91.6)	Satisfaction: 100%	MRI image	10 resident	Test score 74.85 (66.8-73.5)	Satisfaction 50%
Cai <i>et al.</i> , 2019 ^[25]	3D-printed knee	17 students	NA	Knowledge score: 85.03 (10.13)	Accuracy: 80%	Didactic lecture	18 students	test score 70.71 (15.13)	Accuracy 38.9%
Wang <i>et al.</i> , 2020 ^[92]	3D-printed cardiac model	17 students	22.29 (0.85)	Knowledge test score: 6.24 (1.3)	Response time 224.53 (44.13) seconds; Satisfaction 10 (9-10); Accuracy 80 (60-100)	Traditional model	17 students	Knowledge score 7.18 (1.7)	Response time 238.71 (68.46) Satisfaction 10 (9-10) Accuracy 80 (72-88)
Wu <i>et al.</i> , 2018 ^[34]	3D-printed model of wrist, ankle, pelvis and spine	45 students	NA	Test score: Upper limb 7.47 (1.5); Lower limb 7.38 (1.34); Pelvis 6.89 (1.39); Spine 6.93 (1.51)	Satisfaction: 7.49 (1.38); Response time: Upper limb 189.3 (29.5); Lower limb 188.2 (31.1); Pelvis 246.4 (38.9); Spine 237.9 (42.9)	Traditional radiological image	45 students	Knowledge score: Upper limb: 7.24 (1.61); Lower limb: 7.2 (1.56); Pelvis: 4.93 (1.79); Spine: 4.76 (1.61)	Satisfaction: 5.8 (1.3); Response time: Upper limb 193.2 (40.2); Lower limb: 190.8 (42.6); Pelvis: 295.8 (49.4); Spine: 270.3 (54.3)
Awan <i>et al.</i> , 2018 ^[22]	3D-printed hip	11 residents	30	Test score: 35.5 (23.4)		Lecture	11 residents	Test score: 16.4 (15)	
Chen <i>et al.</i> , 2020 ^[12]	3D-printed gastrocolic trunk	23 Interns	NA	Mean difference test score: 47.04 (12.99)	Satisfied 21/23	No intervention	24 interns	Mean difference test score: 32.57 (13.86)	Satisfied 14/24
Al-ali <i>et al.</i> , 2017 ^[21]	3D-printed lip	33 students	NA	Mean difference test score: 44.65 (19.08)	Satisfied 30/33	PowerPoint	34 students	Mean difference test score: 32.2 (11.3)	Satisfied 19/34
Hojo <i>et al.</i> , 2019 ^[29]	3D-printed pelvis for lymph node	17 students	NA	Pretest score: 2.12 (2.28); Posttest score: 7.65 (1.5)	Satisfaction	Text book	17 students	Pretest score: 2.29 (2.54); Posttest score: 6.12 (2.6)	Satisfaction
Hojo <i>et al.</i> , 2019 ^[29]	3D-printed pelvis	17 residents	NA	Pretest score: 2.65 (2.09); Posttest score: 8.47 (1.42)	Satisfaction	Text book	17 residents	Pretest score: 2.35 (1.41); Posttest score: 7.41 (1.7)	Satisfaction
Jones and Seckeler, 2017 ^[28]	3D-printed aorta	17 residents	NA	Pretest score: 25.2 (13.9); Posttest: 62.2 (16.7)	NA	Lecture	19 residents	Pretest score: 19.5 (15.9); Posttest score: 45.1 (12.8)	NA
Bohl <i>et al.</i> , 2019 ^[24]	3D-printed lumbar spine (CT)	4 students	NA	Knowledge score: 9.5 (0.79)	NA	Lecture	4 students	Knowledge score: 6.83 (0.45)	NA

Contd...

Table 2: Contd...

Authors - year	Name of intervention	Total	Mean age with SD	Primary outcome	Secondary outcome	Name of intervention	Total	Primary outcome	Secondary outcome
Su <i>et al.</i> , 2018 ^[36]	3D-printed heart model	32 students	21 (0.57)	Test score: 62.5 (19.04)	Satisfaction 27/32 or 84.4% and confidence 72.19 (14.91)	Seminar	31 students	Test score: 51.29 (17.55)	Satisfaction 16/31 (50%) Confidence level 56.12 (10.55)
Chen <i>et al.</i> , 2017 ^[13]	3D-printed skull	26 students	20 (20-21)	Mean difference of test score: 27 (23-31.625)	Satisfaction 85%	Atlas	26 students	Mean difference test score: 25 (21.75-28.125)	Satisfaction 45%
Smith <i>et al.</i> , 2017 ^[14]	3D-printed bones and lungs	66 students	NA	Pretest score: 4.53 (1.83); Posttest: 7.46 (1.63)	NA	Module Tutorial	61 students	Pretest score: 4.57 (1.83); Posttest 6.52 (1.31)	NA
White <i>et al.</i> , 2018 ^[33]	3D-printed heart	14 residents	28.2 (1.9)	Mean difference: 1.93 (1.3)	NA	Lecture	12 residents	Mean difference: 3.16 (0.6)	NA
White, 2018 ^[33]	3D-printed heart	17 residents	29.3 (2.8)	Mean difference: 2.65 (1.3)	NA	Lecture	17 residents	Mean difference: 2.23 (1.6)	NA
Li <i>et al.</i> , 2015 ^[16]	3D-printed spine	40 students	22.1 (3.22)	Mean score: 7.175 (1.44)	Response time: 375.15 (176.27) seconds	2D CT image	40 students	Mean score: 4.12 (1.32)	22.1 (3.22) Response time 808.06 (240.6) seconds
Lin <i>et al.</i> , 2018 ^[35]	3D-printed skull base	22 residents	25.7 (1)	Mean difference: 9 (1.1)	NA	Atlas	20 residents	Mean difference: 7.3 (1.7)	NA
Tanner <i>et al.</i> , 2020 ^[15]	3D-printed skull (Pterygopalatine fossa)	45 students	NA	Pretest score: 5.71 (2.913); Posttest score: 7.04 (3.04)	Satisfaction	Handout	43 students	Pretest score: 5.44 (2.62); Posttest score 5.56 (2.86)	Satisfaction
Tanner <i>et al.</i> , 2020 ^[15]	3D-printed skull (Pterygopalatine fossa)	15 students	NA	Pretest score: 5.87 (2.64); Posttest score: 10.07 (3.56)	Satisfaction	Atlas	15 students	Pretest score: 5.87 (2.42); Posttest score: 8.27 (2.58)	Satisfaction
Loke <i>et al.</i> , 2017 ^[30]	3D-printed cardiac model	18 residents	NA	Pretest score: 4.3 (1.9); Posttest score: 6 (1.6)	NA	2D drawing	17 residents	Pretest score: 3.8 (1.5); Posttest score: 6.3 (1.2)	NA

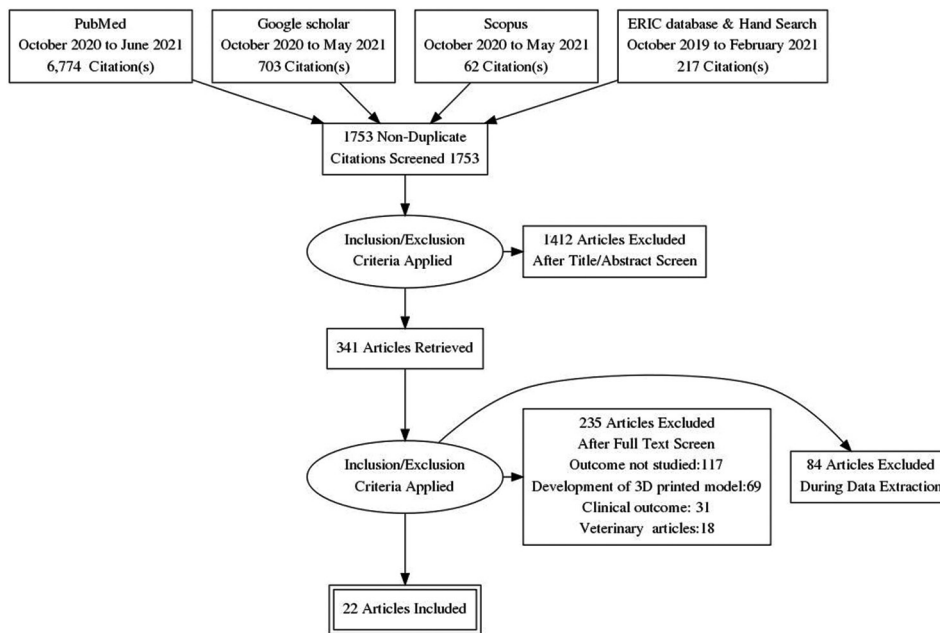


Figure 3: PRISMA flow diagram of search strategy

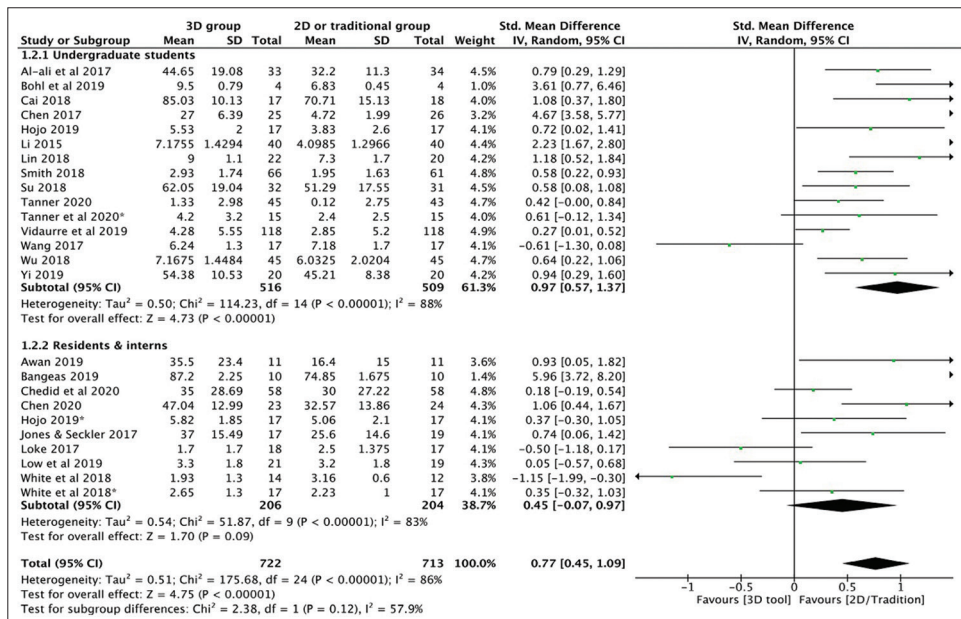


Figure 4: The forest plot; pooled effect size of changes in test score in 3DPM group with reference to 2D or traditional method

studies were symmetrically arranged on both sides of no effect line. Therefore, no missing studies were expected on the evaluation of the plot of SE (SMD) and SMD.

Discussion

Summary of findings

The goal of the study was to examine the benefits and suitability of 3DPM and its comparison with traditional methods for anatomy learning. The current review focused on Kirkpatrick level 2 or Miller’s knowledge and

applied knowledge framework since it is most relevant to the first-year medical, allied health students and trainee residents. According to the findings of these studies, health science students who learnt using it outperformed than students who learned using traditional methods in post-test scores with moderate-to-large effect size. Such findings could not be established for trainee residents due to heterogeneity in the study population and methodologies; these need further studies. Both knowledge and skill domains were tested in residents which could be another possible reason for indifference.

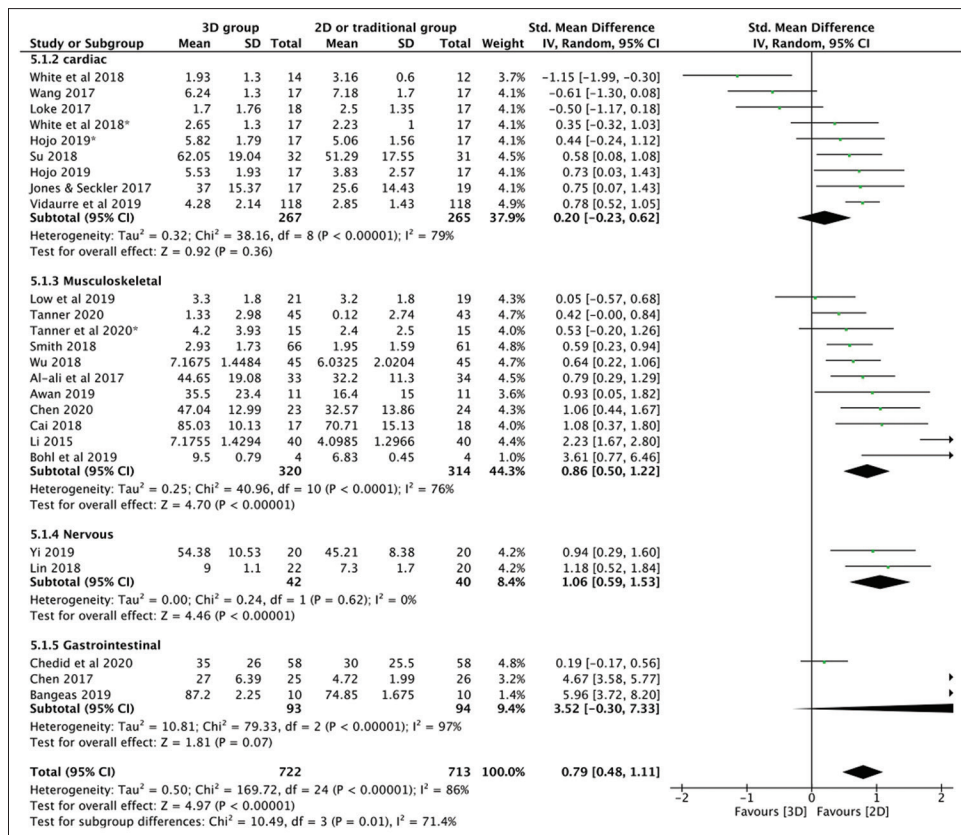


Figure 5: Forest plot evaluating the change in test score based on subgroup of intervention

Moreover, students and residents may not experience similar difficulties in recognizing them in the clinical scenario because of the complexity of structure.^[14] However, in terms of accuracy and satisfaction level, 3DPM is not significantly inferior to traditional. Between the two methods (3DPM vs 2D/traditional), there was no difference in completion or response time. It is superior to traditional methods for short-term retention (based on test score). However, its superiority above traditional models was not established for long-term retention due to paucity of available data. 3DPM is an effective tool for learning anatomy of musculoskeletal and central nervous systems as shown in the current study, but the same could not be established for cardiovascular and peripheral nervous systems because both are difficult to contextualize in 3DPM (like in angiogram, elastography or diffusion tensor imaging). The differentiation of blood vessels and peripheral nerves and their course are difficult to examine in cross-sectional images and 3DPM (which is produced from volume rendering of cross-sectional images).

Yamine and Violato evaluated the effectiveness of physical models (plaster of Paris, or plastic or clay models) in anatomical education. They included 8 studies in their meta-analysis and computed the effect estimates of overall knowledge as an outcome (factual

and spatial knowledge acquisition). The effect estimate was 0.73 (0.353–1.119, 95% CI, $i^2 = 84.7\%$, $P = 0.0002$).^[2] Ye *et al.*,^[9] conducted subgroup analysis based on organ system for 3DPM, claimed superiority of 3DPM for the brain, musculoskeletal, abdominal and trunk muscles except for heart model. Their analysis also captured similarly high heterogeneity (60%–89%). Fleming *et al.* conducted a meta-analysis evaluation of 3DPM among medical students involving 4 studies having 124 participants in the 3D-printed group and 129 in the traditional control group. They computed the effect size (SMD) which was 0.54 (0.29–0.79, 95% CI) without heterogeneity. Furthermore, Fleming *et al.*,^[11] in 2020, calculated the pooled estimate from studies involving resident physicians ($N = 228$ participants). The effect size of the 3DPM for resident physicians was 0.15 (–0.32 to 0.62, 95% CI, $P = 0.53$) with significant heterogeneity. We captured similar results and higher heterogeneity.

Effectiveness of 3DPM models: Possible mechanism based on learning theory

According to Jansen *et al.*,^[37] tangible visualizations of structure have several advantages over on-screen or 2D image visualizations, as it allows for more active perception, leverages nonvisual senses such as touch, integrates with the physical world, and harnesses the interplay between vision and touch to facilitate cognition.

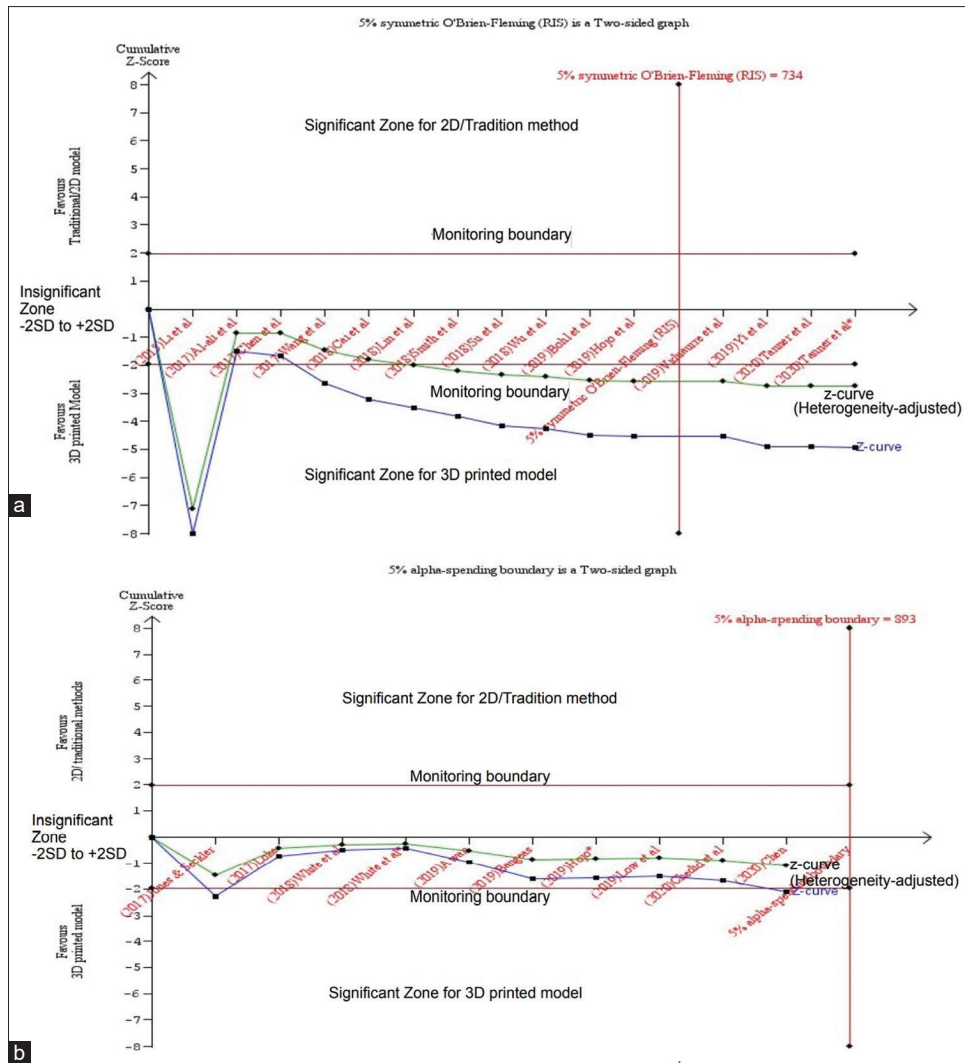


Figure 6: (a) Trial Sequence Analysis (TSA) of 3D printed model among students' population. Cumulative Z-curves (blue color) and penalized cumulative Z-curve (green color); RIS = 734. Total sample size crossed the RIS ($n = 734$). Thus, 3DPM is superior to 2D or traditional method or drawing. No further trials are needed. (b) Trial Sequence Analysis (TSA) of 3D-printed model among residents' population. Cumulative Z-curves (blue color) and penalized cumulative Z-curve (green color); RIS = 893. The total sample size did not cross the RIS ($n = 893$). It is not superior to 2D or traditional models or drawings as green line falls within monitoring boundary. Further trials are needed for confirmation

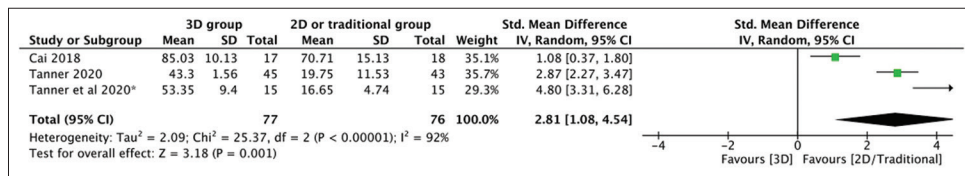


Figure 7: Forest plot evaluating shift in accuracy in 3DPM group with reference to 2D tradition method

Khot *et al.*^[38] turned heart CT data into 3D-printed heart model and evaluated students' engagement. The participants stated that the constructs served as a reward and allowed them to reflect their previous learning experiences. According to goal-setting theory, such rewards are vital in retaining interest in any activity, and reward-based therapies push healthy behaviour change (as extra effort in learning, engagement, and reflection) in students' learning.

Representational insight is the ability to perceive and mentally depict a relationship between a structure and its surroundings.^[39,40] The multi-material and multicolored nature of 3DPM enable them to learn deeper characteristics of structure beyond the simple identification and discrimination. It helped participants to contextualize the structure, create the mental image, and retrieve the information which assists them to apply it in different situations.^[7] Students agreed that 3D

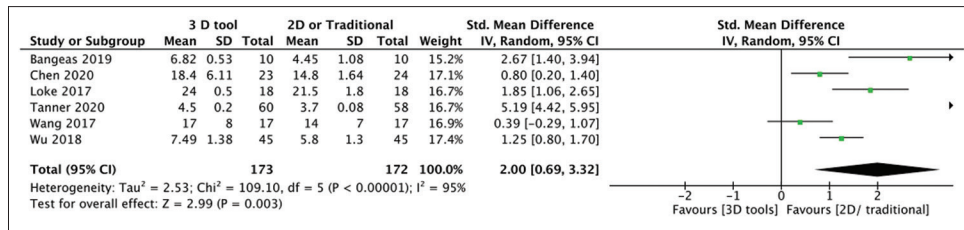


Figure 8: Forest plot of pooled effect size evaluating change in satisfaction score of 3D printed model with reference to 2D or traditional method

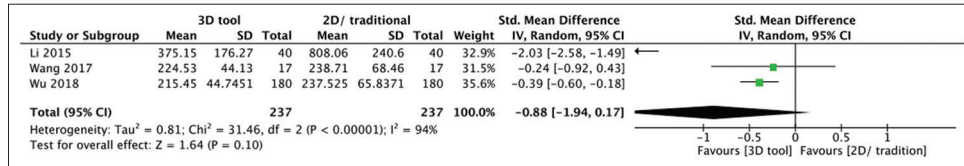


Figure 9: Forest plot of pooled effect size of mean difference of completion time of 3D-printed models with reference to 2D or traditional method

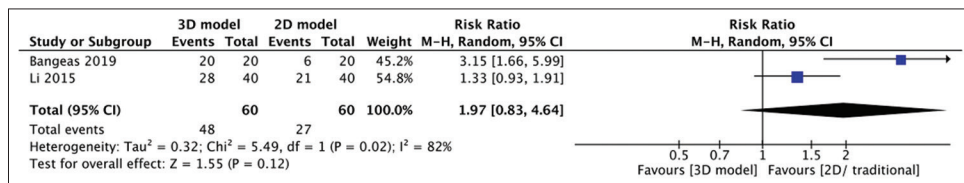


Figure 10: Forest plot of pooled effect size of proportion of subjects felt useful with 3D-printed models with reference to 2D or tradition method

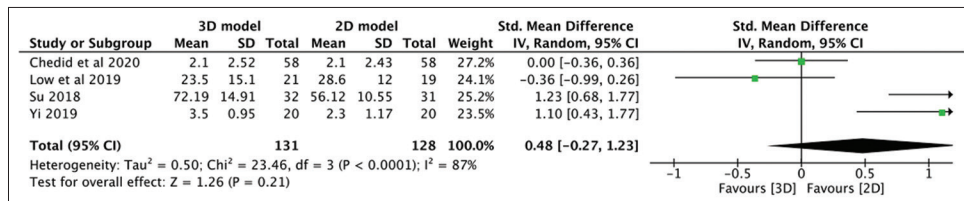


Figure 11: Forest plot of pooled effect size (SMD) confidence level rated by subjects on a Likert scale in 3D-printed models with reference to 2D or traditional method

models will act as a tool of mental rotation and spatial ability to boost their own and peers' understanding, awareness, and motivation.^[41] Previous research has shown that participating in learning activities with peers promotes motivation, enjoyment,^[39,40] intensity,^[42] and out-of-school participation.^[43]

3DPM are an important aspect of the case-based learning process. Actively incorporating such models into the learning environment would be a better strategy.^[44] According to Romanek and Lynch, the core principle of case-based or object-based learning is that appealing with an object or model helps the students' learning. It has been suggested that interlocking the sense of touch with visual perception might aid with memory retention.^[45] In constructivist approach, students' understanding and knowledge are formed via interaction (team work with discussion and debates). Two-dimensional visualizations have the ability only to engage learners at superficial level via passive transmission of information.^[46] They do not foster higher order thinking (analysis, synthesis,

and assessment) and immersion like in 3D models or cadaveric dissection.^[47] Fear, anxiety and discomfort may lower the level of immersion with cadaveric materials. Students had less psychological distress when dealing with 3DPM compared to wet materials due to odorlessness, and dryness.^[13]

Implication of 3DPM in modern curriculum

Thinking, doing, feeling, and reflecting are the processes of learning (Kolb's Cycle). The textual material, presentations, movies, and models are used to introduce new concepts (abstract conceptualization).^[48] In the "thinking" phase of the lesson plan, students' identify structure shown in 3DPM. In order to develop a 3D concept, students should be encouraged to handle printed models and participate in self-directed small group discussions (8–10 students with team leader) employing their understanding and concepts. Participants were encouraged to share their findings with their peers while touching the models. The instructor acted as a facilitator and created core information before

moving on to the high-level (problem solving), utilizing “think-pair-share” cooperative learning methodologies. Finally, students are given time and encouraged to write down major concepts and theories in their own words as reflection. As a result, learners may feel more confident by integrating these innovative technologies into their formal anatomy curriculum.

3DPMs have been widely used in surgical oncology, plastic surgery, dental surgery, neurosurgery, and as a guide for orthopedic surgery. It reduces the surgeon’s stress and operative time, blood loss, and infection rates.^[49] Like cadaveric samples, they have high anatomical and physical rationality and could be used as a training model.^[50] Patient data could be used for printing 3DPM according to the needs of the clinical scenario or even could be customized according to the learning outcomes and students’ needs.^[51] Students would find every new customized model as interesting and challenging which could be a stimulus for self-directed or peer-mediated learning. They would develop a problem-solving attitude and empathy for patients.^[52] These could be a resource for clinical simulation, surgical training, and studying rare diseases.

Disadvantages of 3DPM

Practically, like every technology, it has disadvantages that must be considered. As Khot *et al.* pointed out, too much data might make a model less comprehensible, while too little data can lead the model to lose its intended purpose.^[53] Distraction is another problem, and students may find it difficult to manage the content.^[54-56] Other shortcomings are adaptability, cost, and environmental hazard. Even teachers and mentors are also not acquainted with this technology. But the adaptability issues will gradually vanish with an acquaintance. Its cost, maintenance, and printing materials are still very costly and beyond the reach of developing countries. As of now, it is only available in premier institutes, but its cost will decline in the near future. The printing materials are not bio-degradable and can not be recycled, so it can pose an environmental challenge in the coming days. The dust material coming out during printing and cleaning may pose as a health hazard for the end-user and technicians. Printing time and expenditure fluctuate according to the model of the 3D printer and the printing material, which are other potential challenges.

Limitations and recommendations

The potential limitation of this study was the lack of data from the larger geographical areas (Africa, Australia & South America). The language was another possible limitation because the English manuscripts were more represented than other languages. An adequate number of manuscripts in other languages could not be found even after an extensive search.

Observed heterogeneity is possibly due to inadequate standardization of content of teaching material, and questionnaires. These could be the possible pitfalls even after adequate validation. Although the present study provides the heterogeneity-adjusted effect size of both interventions, the confidence interval of effect size would be narrowed and devoid of heterogeneity if these factors are adequately standardized. Another limitation is the validity of different assessment methods used in the included studies. The most common method of assessment was questionnaire-based closed-ended items. The difficulty and discriminatory indexes and covariance among the items could also be a possible limitation. Multi-arm RCTs or cross-over trials could be conducted in the future to differentiate the effectiveness of 3DPM from other multimodal tools (prosection, cadaveric dissection, or simulating cadavers) of anatomy education. The intent of acquiring anatomical knowledge before the introduction to the official anatomy course, reservation on the complexity of learning topic based on comments of faculties or anecdotal comments of senior students may introduce bias. The most significant feature of 3DPM is adequate haptic feedback, which is highly reliant on the mechanical properties of the printing materials (adequate elastic modulus and tensile strength), type of printers, processing software, and cost. The absence of established techniques for evaluating macro- and microstructure of 3D-printed models was an obvious restriction. Thus future research should focus on standardized methods for evaluating 3D-printed models.

The present study measured heterogeneity-adjusted effect estimates of knowledge acquisition. The pooled estimates calculated from high-quality cross-over studies made it robust and novel. Determining the long-term retention of anatomical knowledge and the behavioral elements associated with clinical skills and patient care may be the subject of future research. The same set of test items was used for both the pre- and posttests to guarantee that both tests were of equal quality and complexity to determine whether or not there was a change. Appropriate steps should be taken to minimize recall bias and carryover effects. The carryover effects must be eliminated by keeping the washout period, using different learning topics, and blinding the participants on the learning objectives.

Conclusion

Despite the above limitations, the current study demonstrates that 3DPM tool is superior to traditional or conventional methods of anatomy teaching and are providing better factual knowledge and satisfaction to the learners. Therefore, 3DPM could be a potential solution for newly established medical institutions and other institutions having fewer numbers of cadavers.

The present review advocates its appropriate use as students' learning resources. The curriculum could be supplemented with this newer technology under guidance for undergraduate students who have limited knowledge and spatial orientation of any structures.

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Ethical statement

Authors have declared that "APA codes of ethics (2017) 1.01 to 10.10. were followed." The data or images from humans or animals were not utilized in this manuscript.

Authors contributions

Adil Asghar: Conceptualization, Search strategies, Statistical analysis, Manuscript Preparation.

Shagufta Naaz: Risk of Bias, Statistical Analysis, Manuscript preparation, Manuscript editing.

Apurba Patra: Literature search, Collection of literature, Shortlisting of manuscripts,

Kumar Satish Ravi: Literature search, Collection of literature, Shortlisting of manuscripts.

Laxman Khanal: Literature search, Shortlisting of manuscripts, Risk of bias, Manuscript Preparation.

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Conflicts of interest

There are no conflicts of interest.

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