DESCRIPTIVE ARTICLE

ASE

Three-Dimensional Printing of Archived Human Fetal Material for Teaching Purposes

Julia C. Young,[1] Michelle R. Quayle,[2] Justin W. Adams,[1,2] John F. Bertram,[1] Paul G. McMenamin[1,2*]

[1]Department of Anatomy and Developmental Biology, School of Biomedical Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, Australia

[2]Centre for Human Anatomy Education, Department of Anatomy and Developmental Biology, School of Biomedical Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, Australia

The practical aspect of human developmental biology education is often limited to the observation and use of animal models to illustrate developmental anatomy. This is due in part to the difficulty of accessing human embryonic and fetal specimens, and the sensitivity inherent to presenting these specimens as teaching materials. This report presents a new approach using three-dimensional (3D) printed replicas of actual human materials in practical classes, thus allowing for the inclusion of accurate examples of human developmental anatomy in the educational context. A series of 3D prints have been produced from digital data collected by computed tomography (CT) imaging of an archived series of preserved human embryonic and fetal specimens. The final versions of 3D prints have been generated in a range of single or multiple materials to illustrate the progression of human development, including the development of internal anatomy. Furthermore, multiple copies of each replica have been printed for large group teaching. In addition to the educational benefit of examining accurate 3D replicas, this approach lessens the potential for adverse student reaction (due to cultural background or personal experience) to observing actual human embryonic/fetal anatomical specimens, and reduces the potential of damage or loss of original specimens. This approach, in combination with ongoing improvements in the management and analysis of digital data and advances in scanning technology, has enormous potential to allow embryology students access to both local and international collections of human gestational material. Anat Sci Educ 12: 90–96. © 2018 American Association of Anatomists.

Key words: embryology education; medical education; undergraduate education; 3D printing; human fetal development; fetus

INTRODUCTION

The majority of anatomical resources and anatomical teaching tend to focus on the adult, particularly the older adult, to a large degree due to sensitivity to working with fetal (including embryonic), and neonatal cadaveric specimens (Brenner and Pais, 2014; Dittmar and Mitchell, 2016). As a direct result, there is often a lack of access to resources at earlier life stages. Historically, fetal and neonatal cadaveric remains were often acquired illegitimately, however, despite these origins, early life specimens were treated quite differently to adult remains, with more destructive dissection such as craniotomy rarely undertaken. In the 1700s and 1800s, fetal and neonatal specimens were highly prized and provided invaluable knowledge to early anatomists and embryologists (Dittmar and Mitchell, 2016). This continued up to the middle of the 20th century, when fetal/neonatal death was rarely formally acknowledged, and medical practitioners could often access the fetal/neonatal remains following the loss or termination of a pregnancy, or death of an early neonate, without any restrictions (Woods, 2009; Dittmar and Mitchell, 2016). These specimens were collected under historically different legislative conditions than prevail in the present day and still comprise a large part of the archived collections in many hospitals and universities (Mitchell et al., 2011). Currently, legislative restrictions mean there is a very low likelihood of procuring new early human life stage specimens. Thus the acquisition of fetal/neonatal materials for research or educational purposes is more

*Correspondence to: Prof. Paul G. McMenamin, Centre for Human Anatomy Education, Department of Anatomy and Developmental Biology, Monash University, Clayton, Australia. E-mail: paul.mcmenamin@monash.edu

Published online 14 August 2018 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/ase.1805

difficult, and changing societal practices tend to now support the formal acknowledgement of fetal/neonatal loss with religious and/or cultural final rites, including burial or cremation of the remains (Woods, 2008, 2009).

In light of this increasingly difficult access to fetal and neonatal specimens, the use of a variety of imaging modalities, e.g., ultrasound, computed tomography (CT) scans, magnetic resonance (MR) imaging (Brenner, 2014; Dittmar and Mitchell, 2016; Jarvis et al., 2016), or idealized plastic casted models have been the major source of non-cadaveric early life materials currently employed in modern medical anatomy teaching. An alternative has arisen through the introduction of high resolution imaging and the production of high quality 3D printed anatomical replicas; an innovative approach that, since its introduction in 2014, has provided a novel addition to classical cadaver-based teaching of human anatomy (Drake and Pawlina, 2014; McMenamin et al., 2014).

Several studies have formally tested the utility of 3D printed material in anatomical teaching, and have indicated that students respond very positively to this approach. Medical students assessed using double-blinded randomized controlled trials show increased recall when exposed to 3D printed anatomical replicas compared to cadaver specimens plus 3D prints (Lim et al., 2016), a finding supported by further study utilizing printed skulls (Chen et al., 2017). Whole adult bodies scanned by high resolution CT, followed by post-scan processing, segmentation, and printing, also elicited significant increases in knowledge retention in comparison with classical, didactic 2D teaching (Smith et al., 2018). These studies therefore provide solid evidence that the introduction of 3D printed human adult anatomical specimens is beneficial to the study of human anatomy.

This report describes a novel approach that provides 3D printed replicas of human embryonic and fetal material as an alternative to presenting actual human materials. In brief, a limited series of intact specimens that were previously largely restricted to archived storage were CT scanned and 3D printed in binder-jetting (powder) based printers. In addition, these scans were digitally segmented, from CT data, to define internal anatomical features including organs and ossified elements of the skeleton of some of these human fetal data sets. Replicas encompassing aspects of this internal anatomy were then printed in a material-jetting printer capable of producing multicolor and multimaterial prints. This was primarily performed to artificially replicate Alizarin red stained fetal material that is valuable in teaching the ossification sequence of the human skeleton. The resulting 3D prints can be readily handled by students and produced in large quantities if required.

MATERIALS AND METHODS

High Resolution Mapping of Fixed Human Gestational Specimens

Nine fixed human embryonic and fetal specimens were selected from the Monash University Centre for Human Anatomy Education archived collection as representatives of a developmental sequence from estimated [crown-rump length, CRL (Moore et al., 2015)] gestational Week 4 to Week 20. The approximate gestational age was recorded on the container and was effectively the only data available. Permission to scan the specimens was obtained from the Monash Centre for Human Anatomy Education, which reposits material in compliance with the Australian Human Tissue Act (HTA, 1982). Specimens were removed from fixative and scanned in a Siemens Biograph 128 slice CT scanner (Siemens, Munich, Germany) with a slice thickness of 0.6mm and slice interval of 0.1mm, yielding an average voxel dimension across the scanned individuals of ~0.2mm.

Segmentation and Rendering of Scanned Images

Computed tomography scans were loaded into the segmentation software package Mimics, version 17 (Materialise, Leuven, Belgium), where automatic thresholding tools were used to develop two dimensional "masks" that model the external body surface and bones based on Hounsfield unit values within the CT scan. For the full organ model (15 weeks) automatic thresholding was used to develop masks that segment the bones and external body, then manual segmentation tools were used to select and mask the heart, lungs, liver, kidneys, gastrointestinal tract, brain, eyes, aorta, and vena cava in each slice of the CT scan data. Each of the individually thresholded anatomical component masks was converted into a three-dimensional tessellated mesh model using the "Calculate Part from Mask" tool. These models were exported as stereolithography (.stl) files.

Printing 3D Specimens

To 3D print the solid external body models, (.stl) files generated in Mimics software were loaded into the digital art program 3D Coat, version 4.7.06 (Pilgway, Kiev, Ukraine) where the skin and umbilical cords (if present) were digitally painted to add color. The resulting color files (.ply) were exported and 3D printed on a ZPrinter® 650 (3D Systems Inc., Burbank, California). This binder-jetting printer uses a gypsum-like plaster material and clear, black, cyan, magenta, and yellow binders to produce a fully colored 3D printed model (see further discussion in McMenamin et al., 2014; Adams et al., 2015). The specimens generated with the ZPrinter 650 were printed at 0.1mm resolution, and took between 45 minutes for the smallest (Week 9) model and 4 hours for the largest (Week 20) model to print.

To print the semi-transparent body, internal organs and skeleton model, the individually segmented (.stl) files generated in Mimics were loaded onto the Stratasys (Stratasys Ltd., Prairie, MN and Rehovot, Israel) 3D printing software Polyjet Studio™, where color and material properties were assigned for 3D printing on the Stratasys J750™—a multicolor, multi-property 3D printer. This printer type employs curable resins that are ejected through nozzles onto the print bed, then exposed to specific wavelength UV light to cure. This additive manufacturing method allows for object components to be printed with different material properties across the whole object. The external body surface of the fetus was printed in Stratasys Tango Plus material (a clear, soft-touch, UV cured resin, (SKU: OBJ-03224, Stratasys) and the skeleton was printed using Stratasys Vero Magenta material (a hard, opaque, UV cured resin, SKU: OBJ-03299, Stratasys). The clear body with organs was printed as above, but each organ was assigned a different color and printed using a combination of Stratasys Vero Magenta, Yellow and Cyan resins (SKU: OBJ- 03299, OBJ-03302, OBJ-03325, Stratasys). The print time for this specimen on the Stratasys J750™ 3D Printer was 7 hours and 48 minutes at a resolution of 0.027mm.

RESULTS

Selection and Scanning of Original Archived Material

A series of archived human embryonic and fetal specimens judged to be in good condition was selected for high resolution scanning from the Monash Centre for Human Anatomy Education collection to represent a broad gestation series. Digital renderings by the Mimics software algorithm of each fetus are presented (Fig. 1). Notably, these 3D renderings allow for dynamic interaction with the image to show all angles of the original sample, as represented in Figure 1 (specifically, Weeks 12–20), where two perspectives of the specimen are shown.

Gestational Series—Single Material 3D Surface Prints

As an initial test case, a fetus at 20 weeks gestation underwent high resolution scanning, image processing/rendering, and finally printed. Figure 2 shows the sequence of events from initial digital file, to processed image, and the powder printed replica of the fetus. Several examples were subsequently selected from the gestational series to be printed to represent relative size differences through the first and second trimester of gestation (Fig. 3). First trimester (Weeks 9–13) and second trimester (Weeks 15–20) were printed as two separate series. These prints were generated at the correct size ratios within each trimester grouping based on the approximate CRL of each original fetus, and are presented here with the associated fetal age indicated (Moore et al., 2015). This series was printed as solid external body models in the colored powder material. It is estimated that the approximate cost of materials ranged from AUD$30.00 (Week 9 print) to AUD$215.00 (Week 21 print). This does not include labor costs or equipment cost recovery (which is highly variable by institution).

Multimaterial 3D Print with Internal Anatomy

Manual segmentation of digital fetal images was performed on selected fetuses where internal organ structure and morphology had been well preserved as observed on CT scans. From this series, a 15 Week fetus with excellent preservation of internal structures underwent extensive processing and analysis. That information is presented here as a deconstructed data image series (Fig. 4). The ability to print with mixed transparency/opacity allowed for internal fetal structures, including the skeletal system and major internal organs to be readily visualized.

DISCUSSION

The introduction of 3D printed materials to anatomy education has elicited a great deal of interest and uptake globally by medical schools (see discussion in Drake and Pawlina, 2014; McMenamin et al., 2014; Lim et al., 2016; Cornwall, 2016; Chen et al., 2017; Smith and Jones, 2018; Smith et al., 2018). Although discussion to date has focused primarily on the replication of adult human structures, described here is a novel approach of creating high fidelity copies of human development using CT imaging and 3D printing.

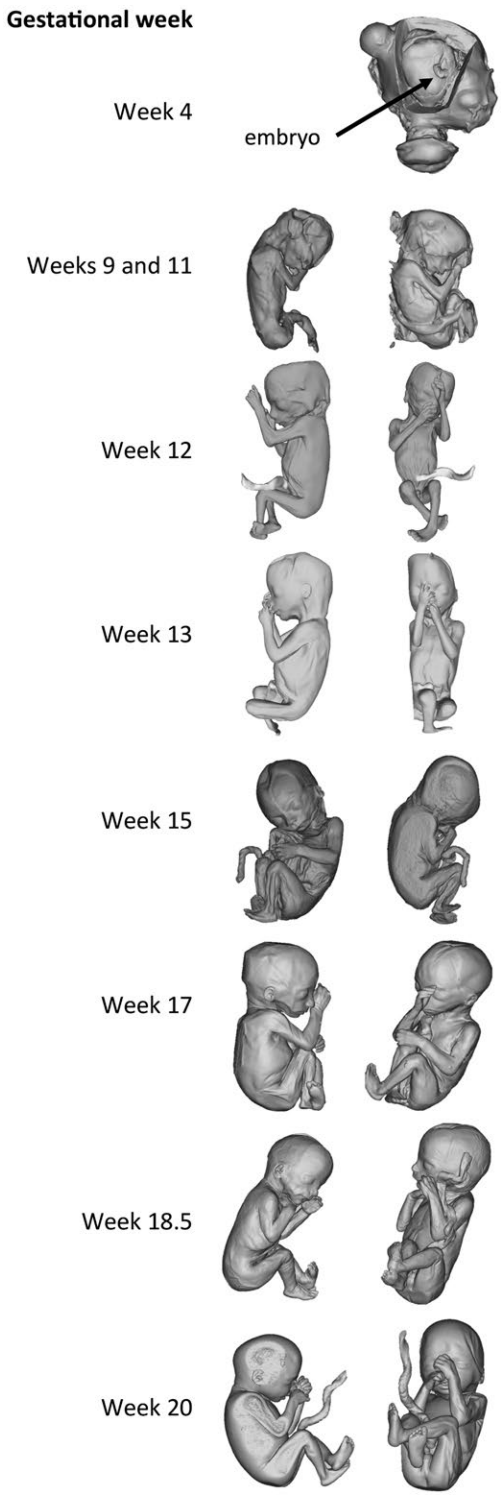

Figure 1.

Digital imaging and 3D rendering of embryonic/fetal scans. A series of nine embryonic/fetal fixed samples were CT-scanned and are presented here as a gestational series of digital renderings. Ages were estimated from a combination of the approximate crown-rump lengths (CRL) and sample history, where available. Two perspectives of the renderings from Weeks 12–20 are presented, to highlight the dynamic interaction possible with these 3D images. Presentation of the age series also highlights external morphological development through gestation.

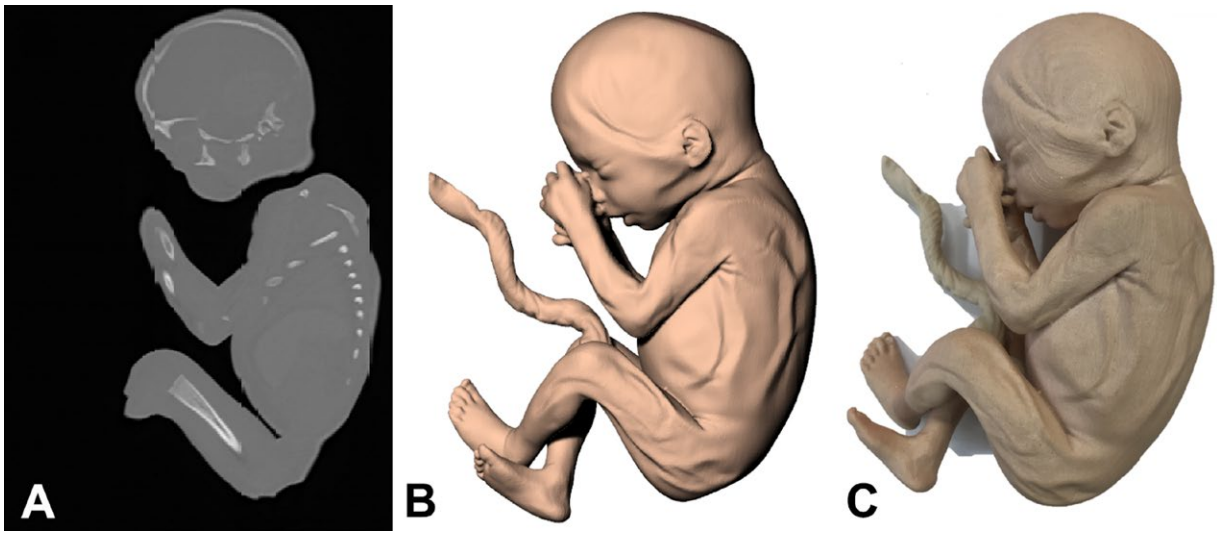

Figure 2.

Human fetus at 20 weeks gestation: Week 20 fetus was selected for an initial test of the high resolution CT scanning and printing process. Presented here is the sequence of events required to proceed from the initial raw data file to the printed replica **A**. Depiction of the raw, high resolution CT scan data from the Week 20 fetus. **B**, Image resulting from stereolithography (.stl) file processing of the raw CT scan data, digitally rendered to show clear surface detail. **C**, Printing of the high resolution rendered image as a 3D gypsum plaster replica.

Studies have shown that students experience particular difficulties when attempting to visualize anatomical structures in 3D (Kramer and Soley, 2002). Using a variety of different teaching materials, particularly those focused on improving thinking in three-dimensional spatial orientations, have already been shown to lead to improved outcomes for students (Lim et al., 2016; Chen et al., 2017; Smith et al., 2018). While it is possible to illustrate the stages of human fetal development with 2D images, anatomy in 3D printed format from actual data will be fundamentally more realistic than textbook illustrations. The approach presented in the current study also has the advantage that it minimizes potential damage to the original preserved cadaveric specimens from which the replicas are derived. This application of 3D printing technology allows students the rare experience of observing and handling accurate reproductions of human fetuses. The replicas described here would also be appropriate for educational contexts in which original specimens are not

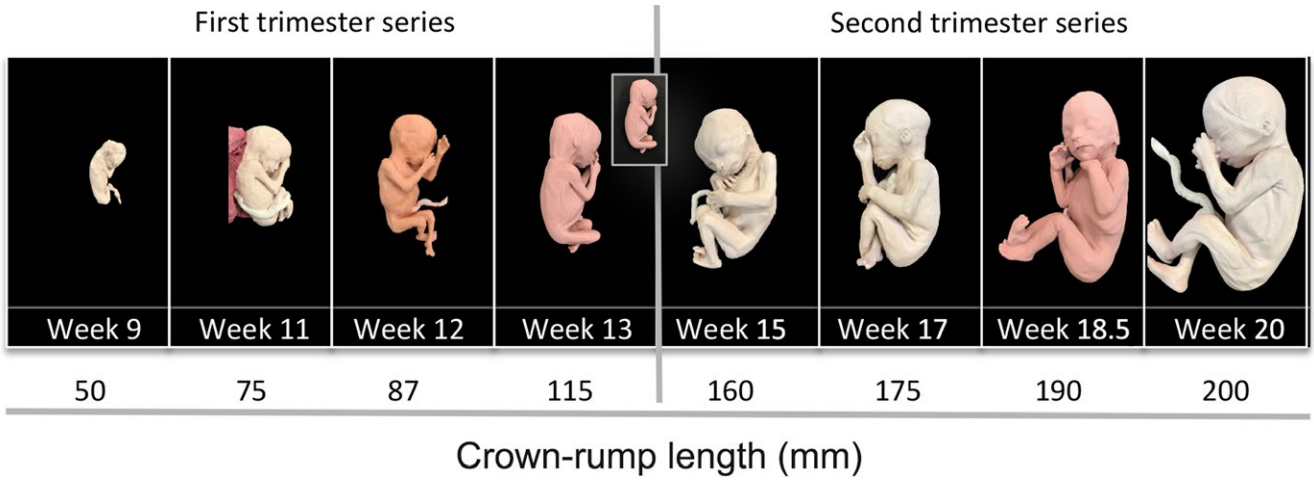

Figure 3.

Printed 3D human gestational series. A selection of the initial fetal gestational scans were chosen for printing as solid external body replicas presented at relative approximate crown-rump lengths (CRL) through a first trimester set (here, Week 9–13), and a second trimester set (here, Weeks 15–20). Image inserted in Week 13 indicates Week 13 print size-corrected relative to the Week 15 print. Print sizes were internally consistent within each set.

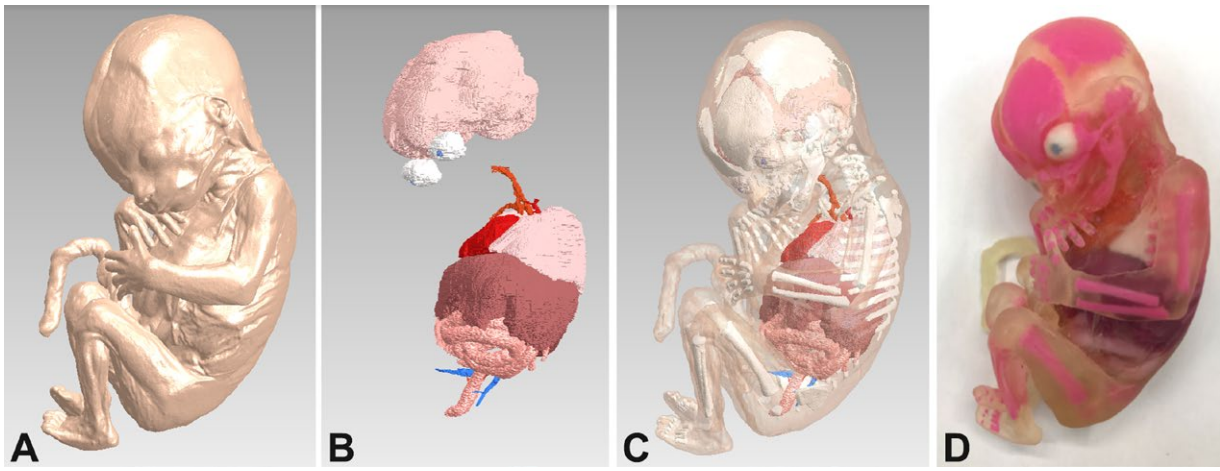

Figure 4.

Week 15 human fetus—full analysis: Week 15 human fetus was CT-scanned, and the high resolution digital data used to segment internal and external hard and soft structures. Presented are: **A**, Week 15 fetus surface detail image, generated from digitally rendered (.stl) processing of the raw CT scan data. **B**, CT data was then processed to identify internal anatomy. Major organs, including the brain, eyes, major arterial structures, liver, lungs, large intestine, and kidney were readily identified via digital segmentation of the processed data. **C**, Composite images were generated to integrate surface detail, internal organs, and skeletal structures. **D**, Composite data files presented in panel C were used to direct printing of multimaterial fetal replicas with internal structures, including major organs and the developing skeletal system clearly visible.

available, such as hospital environments, teaching institutions without Human Tissue Act clearance or in contexts where existing collections simply do not include human embryonic and fetal materials.

The choice of printing materials is also an important consideration both for teaching and for enhancing the educational potential for these 3D printed replicas of human fetal development. While the existing gypsum-plaster or plastic powder-type materials are well-suited for printing whole body forms (as presented here), and the mix of soft/transparent and hard/opaque cured resins are reasonably appropriate for illustrating the position, size, and shape of internal anatomical detail for teaching, improvements still need to be made in printing materials for potential future applications like surgical education and training. Currently, the shore hardnesses of materials used in 3D prints do not approach the Young's modulus of elasticity or Shore hardness of living human tissue, nor are printers yet advanced enough to perform well in printing transitional regions such as the interface between soft and hard tissues. However, with the interest and clear benefits of these approaches, there is a strong drive to push advances in this technology.

Printed 3D specimens have been used to train specialists and clinicians (e.g., Adams et al., 2015; VanKoevering et al., 2015; Li et al., 2017; Loke et al., 2017), and to plan a range of surgical procedures in areas as diverse as hepatobiliary intervention (Javan and Zeman, 2018), nephrectomy (Golab et al., 2017), treatment of osteogenesis imperfecta (Eisenmenger et al., 2017), and both cardiac (Bartel et al., 2017) and spinal surgery (Cramer et al., 2017). This research has highlighted the potential for 3D printing to equally contribute to the development of competency in fetal and early childhood surgery, particularly as a high skill field of surgery, and where the opportunities for skills enhancement may be very limited. There are examples already where the use of printed anatomical structures in surgical training has been explored for pediatric surgery for cleft palate pathologies by authors of the current study (Lioufas et al., 2016), and developmental abnormalities of the ear, where surgery may involve both soft and hard tissues and close proximity to facial nerves (Barber et al., 2016). With access to digital data spanning a broad spectrum of fetal ages, the underlying data developed in the present study can be translated into several different printed formats, including multimaterial prints and 3D print-guided multimaterial simulators for practicing fetal surgery on 3D prints at appropriate stages of human development, as has been done for neurocranial surgical simulation (amongst other applications) (Waran et al., 2014; Ryan et al., 2016, 2015; Tai et al., 2015). In addition, there is future scope for inclusion of specimens with rare pathological issues and/or examples of developmental disorders that would also comprise an important group to integrate into the teaching of human development and surgical training throughout the gestational period.

Study Limitations

Using the approach described in the current study, both surface anatomy and internal anatomy fetal prints have been presented to undergraduate students concurrent with the original potted specimens from which they were derived. Future reports should provide a formal quantitative survey of both students and teaching academics, designed and based on informal observation of these initial interactions. These surveys will determine, importantly, the pedagogical impact of these specimens on the teaching of fetal anatomy.

CONCLUSIONS

The integration of 3D fetal prints into teaching curricula can not only enhance the learning of human development, but also allow flexibility in how data is translated into 3D printed specimens (e.g., selection of materials, scaling of specimens) and reduce the potential for accidental loss of irreplaceable original specimens. Advances in high resolution scanning technologies concurrent with improvements in processing and rendering large scale digital data will continue to support and enhance this new approach to teaching human developmental biology and gestational anatomy.

ACKNOWLEDGEMENTS

The authors wish to acknowledge Stratasys Ltd., for access to the Stratasys J750™ 3D Printer for beta testing.

NOTES ON CONTRIBUTORS

MICHELLE R. QUAYLE, B.Env.Sc.Mgt. (Hons.), is a research and technical assistant for the Centre of Human Anatomy Education in the Department of Anatomy and Developmental Biology, Faculty of Medicine, Nursing and Health Sciences at Monash University, Clayton, Australia. She researches 3D modeling techniques and runs the Centre for Human Anatomy Education's 3D Printing Laboratory.

JUSTIN W. ADAMS, Ph.D., is a senior lecturer and Deputy Director of the Centre for Human Anatomy Education in the Department of Anatomy and Developmental Biology, Faculty of Medicine, Nursing and Health Sciences at Monash University, Clayton, Australia. He teaches human and comparative anatomy to medical and science undergraduate and postgraduate students and his research interest is in comparative anatomy and applications of 3D imaging and quantification.

JOHN F. BERTRAM, D.Sc. (Med.), is a professor, and recent past Head of the Department of Anatomy and Developmental Biology, Faculty of Medicine, Nursing and Health Sciences at Monash University, Clayton, Australia. He has taught developmental biology to undergraduate and postgraduate medical and science students for over 30 years. His research interest is in human kidney development, and particularly associations between low nephron endowment at birth and chronic cardiovascular and kidney disease.

PAUL G. MCMENAMIN, D.Sc. (Med.), is a professor and Director of the Centre for Human Anatomy Education in the Department of Anatomy and Developmental Biology, Faculty of Medicine, Nursing and Health Sciences at Monash University, Clayton, Australia. He has been teaching human anatomy to undergraduate and postgraduate medical and science students for over 30 years, and his research interests are in the role of immune cells in a range of eye diseases including uveitis, macular degeneration and retinopathy of prematurity, as well as the development and integration of 3D printing technologies in anatomy teaching.

JULIA C. YOUNG, Ph.D., is a senior lecturer in the Department of Anatomy and Developmental Biology, Faculty of Medicine, Nursing and Health Sciences at Monash University, Clayton, Australia. She teaches developmental, molecular, and stem cell biology to undergraduate and masters students in science, biomedical science, and medicine. Her research interest is in developmental reproductive biology.

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