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Placenta Vasculature 3D Printed Imaging and Teaching Phantoms

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Abstract

Three-dimensional printing makes it possible to create patient-specific, complex anatomical geometries that can be used for training, teaching and surgical planning. The human placenta is a vital organ that transports nutrients from the mothers' uterine circulation to the fetus via a complex vasculature. Complications of the fetal vasculature are increasingly being imaged with ultrasound and treated before birth using invasive fetal therapy. There is a need for human placenta training phantoms such as placental anastomoses that occur in monochorionic twin pregnancy and can cause twin-to-twin transfusion syndrome and fetal death, if untreated.

In this study we developed two phantoms based on the human placenta using 3D printing technology: an ultrasound imaging phantom and an anatomical teaching model.

Introduction

In recent years, the use of three-dimensional (3D) printing has greatly increased in biotechnology, medical science and, neuroscience due to its versatility in creating a wide range of geometries [1, 2]. It has enabled the production of complex anatomical models such as patient-specific parts that can be used for teaching, training and surgical planning [3-5]. 3D printing is also of interest for developing ultrasound or optical imaging phantoms. [6, 7] In this work, we apply 3D printing technology to create both anatomical teaching models and imaging phantoms of the human placenta.

The human placenta has a complex vasculature system that passes oxygen and nutrients from the mothers' blood supply to the fetus. For fetal medicine and fetal surgical specialists, understanding the anatomy of the placenta is a pre-requisite to properly acquire and interpret placenta ultrasound images. 3D models of the placenta could be a useful tool in teaching while imaging phantoms could be used for procedure training and for validation of new fetal imaging and fetal surgical modalities. Appreciation of the fetal placental circulation is particularly important for successful treatment of twin-to-twin transfusion syndrome (TTTS) a condition that affects 20% of monochorionic twin pregnancies. TTTS is caused by a net transfusion of blood across anastomosing fetal placental vessels in twins that share a placenta. Untreated it causes the death of one or both fetuses in 90% of cases [8-9].

Ultrasound imaging is commonly used from early pregnancy to provide information about the anatomy and physiology of the fetus and placenta, as its safety profile is excellent (Figure 1).

Figure 1 *Ultrasound imaging in pregnancy*

Ultrasound imaging phantoms have proven to be useful for training doctors to perform interventional procedures [7, 10]. Training with realistic phantoms provides invaluable experience and confidence before performing the first in-human procedures, and eventually reduces operational time [10]

In this context we developed two phantoms based on the human placenta using 3D printing technology: an ultrasound imaging phantom and an anatomical teaching model.

Methodology

Ultrasound imaging phantom

The ultrasound phantom was realised using a high-resolution digital single-lens reflex (DSLR) picture of a term healthy human placenta (Fig. 2). This placenta was collected after a Caesarean section delivery at University College London Hospital with written informed consent from the mother, as approved by the Joint Committees on the Ethics of Human Research (08/H0817/07 amniotic fluid and placental stem cells). After delivery of the baby, the umbilical cord was immediately clamped to preserve the maximum amount of blood inside the placental fetal vasculature.

From the DSLR image of the placenta, tracings of the arterial and venous vessels were created using Inkscape software (OpenSource, inkscape.com). These tracings were used to define the direction and the diameter of the vessels. A planar 3D tubular structure was designed using the loft utility function to recreate realistic arterial and venous vasculature systems as shown in Figure 3a, b. FreeCAD (Juergen Riegel, Werner Mayer, Yorik van Havre, OpenSource, freecad.com) was used as the Computer Aided Design software.

As the available 3D printed materials strongly attenuate ultrasound, unlike placental tissue, we chose to use 3D printed moulds filled with a material that is ultrasonically transparent and at the same time mimics the tactile feedback of tissue. Each vasculature mould was designed using Boolean functions in FreeCAD and consisted of top and bottom parts. The blue circles in Figure 2 c, d represent the holes for M4 screws to keep the two parts of the moulds tightly fixed together.

Stereolithographic (STL) files of the moulds were generated and sent to the additive polymer resin Objet printer (Objet 30 Pro, Stratasys, UK) (Fig. 3b). All the moulds were made of a rigid opaque white material with a gloss finish (VeroWhitePlus RGD835, accuracy <0.1mm). As the printing material is expensive, the area of interest was reduced (see red squares in Fig 2a, b). To address the lifetime limitation of typical Agar-based phantoms observed in previous studies, we used oil-based gel wax for the mould filling material. This material was tested under ultrasound imaging and assessed mechanically and did not appear to degrade even after 6 months. In order to create a complex vasculature, two 3D printed moulds were filled with gel wax material that was melted using heat plate and mixed with red or/and blue colour ink representing arterial and venous blood. A degasser (Thermo Fisher Scientific, Waltham, USA) was used to remove trapped bubbles. In addition, a lacquer spray was applied to the surface to avoid diffusion of different colour vessels within a phantom. To make the phantom more visible in ultrasound, 0.5% scatter glass microspheres roughly 65 µm diameter from 3M (3M, Bracknell, UK) were added. The uniform mixing of microspheres in the phantom were achieved with a sonicator (Model 120 Sonic Dismembrator, Fisher Scientific, Hampton, USA).

To evaluate the realism of the imaging phantom in ultrasound imaging, it was inserted in a box that was half-filled with water such that the vasculature was in contact with water. Ultrasound gel was then placed on the exposed side of the placental model and ultrasound images were taken using an L14-5 clinical probe on ultrasound machine (Sonix MDP, Ultrasonix, Vancouver, Canada). The diameters of the vessels were estimated using the same machine.

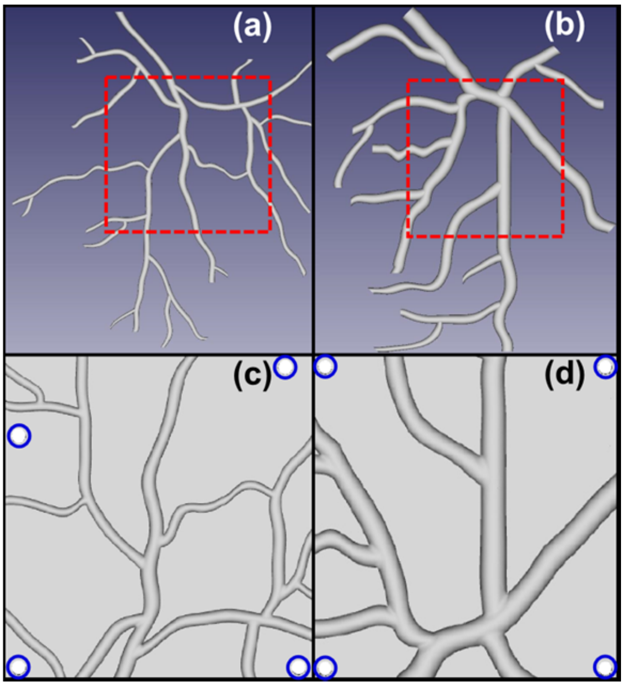

Figure 2 ***(a)*** *The arterial and* ***(b)*** *venous vasculature of human placenta and corresponding moulds* ***(c)*** *for artery and* ***(d)*** *vein designed in FreeCAD. Red squares show the region of interest. Blue circles correspond to holes in the moulds used for screws to fix two halves of the mould together.*

Anatomical teaching model

In addition to the imaging phantom, we developed an anatomical teaching model of the human placenta that can be used for teaching students and junior clinicians.

The anatomical teaching model was developed by scanning a human placenta donated for research as above, using a 3D scanner (Artec Space Spider, Artec 3D, Luxembourg). The acquired stl file was sent to Cura software where gcode file was generated. The model was printed using an extruded thermoplastic polymer printer (Ultimaker2, Ultimaker, Chorley Lancashire, UK) with a Polylactic Acid (PLA) filament material (PolyMax, Polymakr, Changshu, China, accuracy >0.1mm). The model was printed with 20% infill density, 60 mm/s print speed, 120 mm/s travel speed and required 14 m of material. A raft option was chosen to have a better adhesion of the model to the printing surface. The model was painted with acrylic paints to highlight the vasculature of human placenta.

Results

In this work we developed two phantoms replicating a human placenta (Fig. 3 and Fig. 4).

The ultrasound imaging phantom (Figure 3) represents a human placenta with arteries sized from 0.8 mm to 5 mm in diameter; the vein diameters were double that of the arteries. The achieved diameters were within 0.001 mm standard deviation for arteries and 0.015 mm for veins. The phantom was compared to the real placenta and assessed on ultrasound where it was found to have a very similar appearance to the placenta *in vivo* (Fig. 3d, e).

The anatomical teaching model is demonstrated in Figure 4. Arteries and veins in the model correspond very well to the vasculature of the real placenta. The model took 22 hours to

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print out and cost only £5 to produce. The final dimensions of the model were 185 mm x 164 mm x 40 mm.

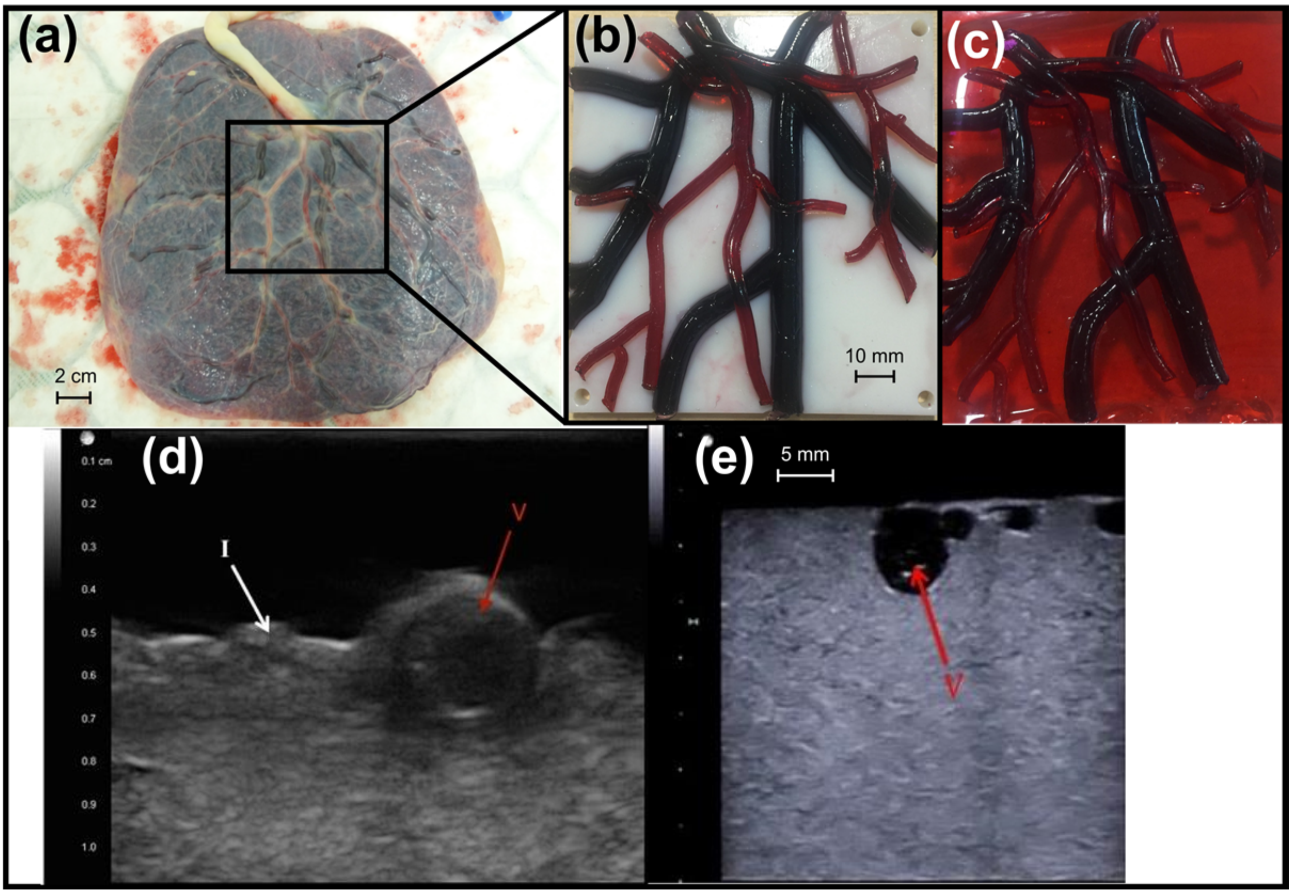

Figure 3 ***(a)*** *A photograph of human placenta,* ***(b)*** *3D printed moulds with the gelwax vasculature of human placenta,* ***(c)*** *an ultrasound image of the phantom,* ***(d)*** *an ultrasound image of the human placenta and* ***(e)*** *of the imaging phantom. The placenta (d) shows some indentation (I) on surface and the vein (V) is slightly less embedded than that shown illustrated by the phantom (e). The surface of the placenta modelled in the phantom is smooth.*

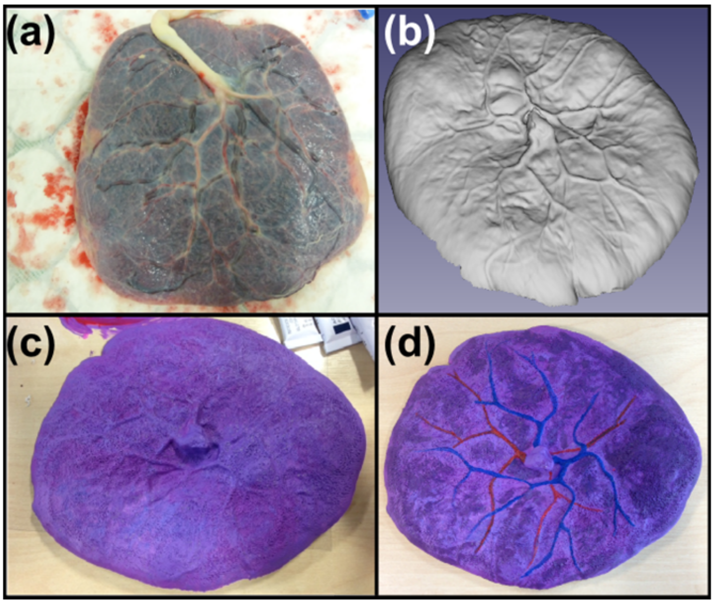

Figure 4 ***(a)*** *A photograph of human placenta,* ***(b)*** *a scanned mesh file of the phantom,* ***(c)*** *3D printed human placenta painted in purple color using acrylic paint,* ***(d)*** *the final teaching model of human placenta*

Discussion

We have demonstrated an affordable method to produce realistic phantoms of the human placenta for ultrasound imaging and teaching purposes. The ultrasound imaging phantom was fabricated using gel wax material that proved to be effective as a tissue-mimicking material. As gel wax has a 95% of oil content there are no problems with dehydration and shape change, problems that tend to occur with Agar based phantoms. The material is also non-toxic and chemically stable. The ultrasound appearance of the imaging phantom is very similar to imaging of a real placenta *in vivo*. As the phantom was derived from a high resolution photograph of the fetal surface of the placenta, it represented only those vessels situated on the superficial part of the placenta. This is not a problem for simulation of fetal therapy since it is the fetal surface of the placenta that is important for therapy. The moulds fabricated using 3D printing for the development of vessels of the vein and arteries are robust, reusable and reproducible although they are costly. They are very easy to use to replicate the real anatomy of the placenta. This phantom does not represent the full placenta but only a section of it and there is no blood flow in this phantom which is the subject of future work. Candle dye used for colouring vessels was found to diffuse in the phantom but this was prevented by the application of lacquer that prolonged the life of the phantom.

The anatomical teaching model is cost-efficient and light weight. It can be useful as a teaching material. The STL file of the placenta can be distributed electronically and reprinted using any available printer. More information on how to create teaching phantoms based on imaging data can be found at www.3d-med.co.uk.

Conclusion and future work

In this paper we demonstrated a gel wax based ultrasound imaging phantom and a PLA anatomical teaching model that could be used for training, teaching and surgical planning. Both represent the human anatomy of the placenta very well.

In the future, an imaging phantom representing a full placenta with all its vasculature will be fabricated, as well as phantoms that can mimick blood flow within the placenta. There is still room for improvement of the phantoms including the development of a 3D ultrasound imaging placental phantom that represent deep vessels as well as the superficial surface vessels. Finally, further involvement of clinicians is required to give constructive feedback on developed phantoms.

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Keywords

3D printing, human placenta, ultrasound imaging phantom

Author Biography

Daniil Nikitichev has earned a PhD degree from University of Dundee (2012) in Laser Physics. The same year he joined the University College London in London, UK. He has been working with a photoacoustic ultrasound system for ex-vivo and in-vivo imaging of the tissues and organs. His research topics include 3D printing, acoustic properties of 3D printed materials, acoustic sensors, photoacoustic imaging, optical and photoacoustic phantoms.

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