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Additive manufacturing models of fetuses built from three-dimensional ultrasound, magnetic resonance imaging and computed tomography scan data

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KEYWORDS: additive manufacturing; computed tomography; fetus; magnetic resonance imaging; ultrasound

ABSTRACT

Objective *To generate physical fetal models using images obtained by three-dimensional ultrasonography (3DUS), magnetic resonance imaging (MRI) and computed tomography (CT) to guide additive manufacturing technology.*

Methods *Images from 33 fetuses, including three sets of twins, were used. Fifteen fetuses were normal and evaluated only by 3DUS. Eighteen cases had abnormalities such as conjoined twins, tumors, aneuploidy, skeletal abnormalities, central nervous system abnormalities and facial or thoracic defects. Scans were performed using high-resolution 3DUS. In cases of abnormalities, MRI and CT were performed on the same day as 3DUS. The images obtained with 3DUS, CT or MRI were exported to a workstation in DICOM format. A single observer performed slice-by-slice manual segmentation using a digital high-definition screen. Software that converts medical images into numerical models was used to construct virtual 3D models, which were physically realized using additive manufacturing technologies.*

Results *Physical models based on 3DUS, MRI and CT images either separately or combined were successfully generated. They were remarkably similar to the postnatal appearance of the aborted fetus or newborn baby, especially in cases with pathology.*

Conclusion *The use of 3DUS, MRI and CT may improve our understanding of fetal anatomical characteristics, and these technologies can be used for educational purposes and as a method for parents to visualize their unborn baby. The images can be segmented and applied separately or combined to construct 3D virtual and physical models.*

INTRODUCTION

Advances in image-scanning technology have led to vast improvements in medicine, especially in the diagnosis of fetal anomalies[1]. In general, three main technologies are used to obtain images within the uterus during pregnancy – three-dimensional ultrasonography (3DUS), magnetic resonance imaging (MRI) and computed tomography (CT). The development of ultrasound scanning during the 1960s opened a new window into the study of the fetus. It is currently the primary method for fetal assessment during pregnancy because it is patient friendly, useful, cost-effective and considered to be safe. Many centers are exploring 3DUS because of the life-like images of the fetus it provides[2–5]. MRI is a non-invasive method that has been used in obstetrics since the 1980s. It offers high-resolution fetal images with excellent contrast that allow visualization of internal tissues[6]. When ultrasonography yields equivocal results, MRI is generally used, because it provides additional information about fetal abnormalities and conditions in situations where ultrasonography cannot provide high-quality images[7–10]. CT is used only in specific cases of suspected fetal malformation, particularly those related to the skeleton, because of potential risks associated with exposure of the fetus to radiation. Its use during pregnancy must be adequately justified and its application is limited to specific

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pathologies such as bone dysplasia, which can, in some cases, be difficult to diagnose by ultrasound, especially in the absence of a family history of the disease[11].

Additive manufacturing (AM) is the automatic, layer-by-layer construction of physical models using solid free-form fabrication. The first AM techniques were used in the late 1980s to produce models and prototypes. The use of AM in the biomedical sector has increased steadily over the past decade. Different uses have been reported widely in the medical literature[12–14], but little has been published on its application to the gravid uterus, so we applied AM technology to fetal images obtained by 3DUS, MRI and CT.

METHODS

From September 2007 to May 2009, 33 fetuses, including three sets of twins, were selected from cases evaluated in Rio de Janeiro and London. All cases were scanned by 3DUS in the first, second and third trimesters, and 15 normal fetuses were evaluated only by 3DUS. Morphological abnormalities were first imaged by 3DUS in 18 fetuses. Central nervous system and thoracic abnormalities were indications for MRI, and skeletal malformations were indications for CT (Table 1). MRI and CT reinforced the previous preliminary 3DUS findings, and diagnoses were confirmed postnatally.

A high-resolution ultrasound probe with harmonic imaging (4–8-MHz transducer, Voluson 730 Pro/Expert system, GE Medical Systems, Zipf, Austria) was used to perform all the 3DUS scans transvaginally and/or transabdominally. MR images were acquired using a 1.5-T scanner (Magneton Avanto, Siemens, Erlangen, Germany), with body coil. The MRI protocol was a T2-weighted sequence in three planes of the fetal body (HASTE; TR shortest, TE 140 ms, field of view 300–200 mm, matrix 256 × 256, slice thickness 4 mm, acquisition time 17 s, 40 slices). Examination times did not exceed 30 min. CT was performed with a multislice 64 scanner (Philips, Solingen, Germany) with parameters 40 mAs, 120 kV, 64 slices per rotation, 0.75 pitch and 0.75 mm slice thickness. This corresponds to a mean radiation dose of 3.12 mGy (CT dose index weighted) to the fetus.

All 3DUS, MR and CT images were exported to a workstation in DICOM format for manual, slice-by-slice segmentation by a single observer using a digital high-definition screen tablet (Cintiq Wacom, Tokyo, Japan). The 3D structure of the fetus was reconstructed by generating skinning surfaces that joined the resulting profiles. Software that converts medical images into numerical models (Mimics v. 12, Materialize, Leuven, Belgium) was used for 3D virtual model reconstruction, and the model was exported into a standard triangular language (STL) format and converted into an 'OBJ' extension for adjustment using 3D modeling polygonal software (Autodesk Mudbox, San Francisco, CA, USA). Using this software, the volumetric surface was smoothed, to be later compared and analyzed as a topographic construction. After this procedure, the 3D model was again converted and exported as an STL extension. The model file was opened in Mimics software for correlating the contours of the 3DUS, MR or CT images with the generated 3D surface. The physical modeling process was conducted by resolving the layers of a photopolymerized resin solidified with a laser beam (stereolithography system). For generating physical models, the data from each slice were used to direct the laser beam over the x- and y-axes of the surface of a liquid photopolymer reservoir. The 3D geometry was achieved by hardening the photopolymer and gradually lowering the supporting structure and the physical model was hardened in a special chamber under ultraviolet radiation.

Table 1 Summary of the 18 fetuses with abnormalities

*Case number**	*Gestational age at assessment (weeks)*	*Assessment method*	*Diagnosis*	*Additive technology*
1	34	3DUS/CT	Left femoral hypoplasia	SLA
2	34	3DUS/CT	Left femoral and tibial hypoplasia and left fibular agenesis	SLA
3, 11	28, 26	3DUS/MRI	Chiari II malformation	SLA, Z Corp
5	29	3DUS/MRI	Agenesis of the corpus callosum	SLA, Z Corp
7, 24	32, 28	3DUS	Cleft lip	Z Corp
10	31	3DUS/MRI	Diaphragmatic hernia	SLA, Z Corp
12	26	3DUS/MRI	Alobar holoprosencephaly	SLA, Z Corp
14	34	3DUS/MRI	Hydrocephaly	SLA, Z Corp
15	31	3DUS/MRI	Agenesis of the corpus callosum†	SLA, Z Corp
18	26	3DUS	Down syndrome	Z Corp
22	34	3DUS/MRI/CT	Achondroplasia dwarfism	SLA, Z Corp
23	34	3DUS/MRI/CT	Thoraco-omphalopagus twins	Z Corp
27	35	3DUS/MRI/CT	Legs and right hand amputation and syndactyly	Z Corp
28	30	3DUS/MRI	Sacrococcygeal teratoma	SLA, Z Corp
30	28	3DUS/MRI	Ventriculomegaly†	SLA, Z Corp

*Seventeen cases are shown because Case 23 included two fetuses with thoraco-omphalopagus. †Twin pregnancy with one twin affected. 3DUS, three-dimensional ultrasound; CT, computed tomography; MRI, magnetic resonance imaging; SLA, stereolithography (liquid-based system); Z Corp, Z Corporation Technology (powder-based system).

In some cases, instead of a liquid-based system, we used a powder-based one (Z Corporation Technology, Burlington, MA, USA) (Table 1). This procedure uses a printer head to deposit an agglutination liquid whose composition is similar to plaster as a top layer of the material. As the printer head elevator moves down, additional layers of material can be added and this is repeated until the model is complete. This process does not use a support structure, since the model is positioned inside the powder, which sustains the prototype.

The ethical issues associated with this work were carefully considered. Signed consent for the medical research use of their fetal images was obtained from all parents and approval for this work was obtained from the ethics committee of the clinics. Some results described in this work were used previously to demonstrate and explain physical characteristics to parents or specialists.

RESULTS

The physical models generated were satisfactory in all cases. The mean time and manufacturing cost for each process are summarized in Table 2. CT gave high-resolution images of bony structures with high visual contrast. In general, the segmentation process to separate the fetal skeleton from the uterine walls was carried out automatically by medical imaging treatment software. For CT, we also used manual segmentation to process images of the external surface of the fetus. MR images showed high contrast between internal organs and the external surface. Analysis of the MR images is an interactive process that visually detects the boundaries of the fetal body parts using a digital stylus pen that is applied directly to the computer screen. The resulting image layers of the relevant area are then virtually overlapped to generate a 3D volumetric model. The physical models of 3DUS cases gave excellent impressions of the face, ears, hands and feet, which highlights the possibilities offered by this technique (Figure 1). The main difference between the modeling methods was in the contrast resolution of bony structures and the number of layers available. Typically, more than 100 image slices were available from CT or 3DUS, and 20–30, with a thickness range of 3 to 6 mm, were obtained from MR images. Combined procedures were successfully developed for building physical models, for example using 3DUS and MRI, MRI and CT or using all three methods.

Table 2 Estimated model fabrication times and costs for all 33 fetuses studied

*Case number**	*Estimated time (h)*	*Estimated cost (US$)*
1, 2, 3, 4, 5	22–26	1300–1700
6, 7, 8, 16, 17, 28	2–4	80–120
9, 10	5–7	200–400
11, 13, 19, 20, 21, 24, 25, 26	1–2	30–80
12, 14, 15, 18	4–5	150–250
22	11	800
23	28	1900
27, 29, 30	7–8	280–500

*Thirty cases are presented because there were three sets of twins.

In case number 24, the fetus of a 32-year-old primigravid woman was evaluated from a fetal ultrasound scan showing a cleft lip at 28 weeks' gestation. A virtual and physical model of the cleft lip – which bore a striking similarity to the 3DUS image – was obtained (Figure 2). Case number 12 was a 34-year-old primigravid woman who was evaluated for fetal alobar holoprosencephaly at 26 weeks' gestation. Virtual and physical models were built using MR imaging combined with 3DUS. A joint file was made modeling the body from MR imaging

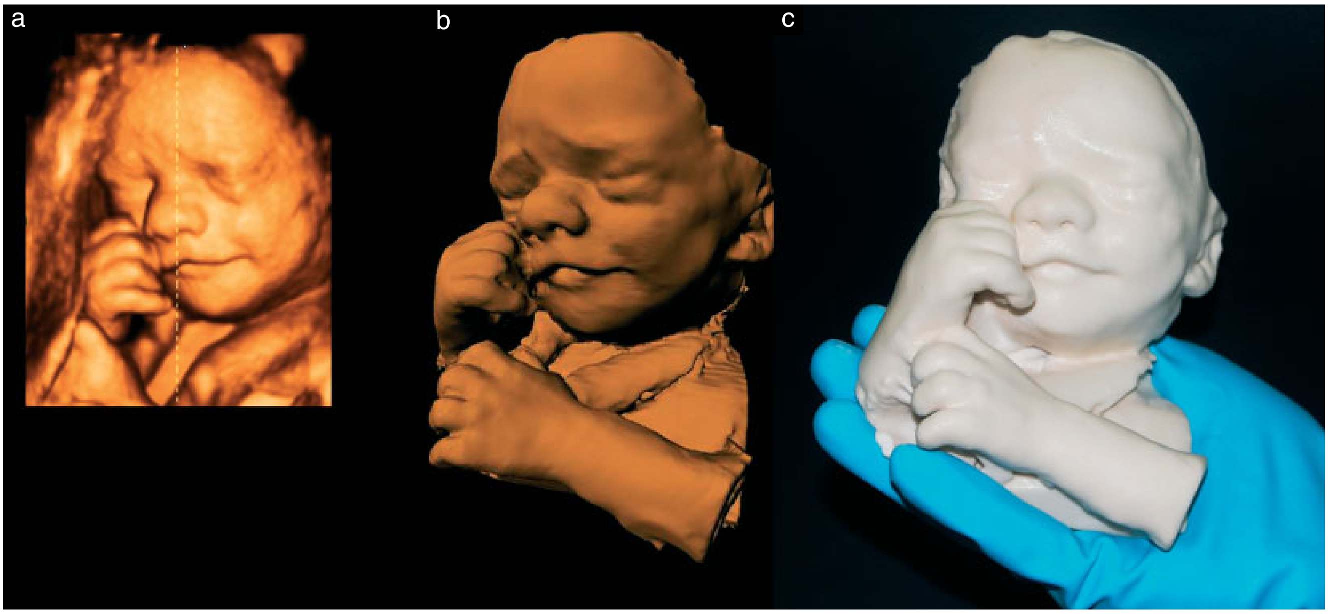

Figure 1 Normal fetus at 26 weeks' gestation. Three-dimensional (3D) ultrasound image (a), mathematical 3D virtual image (b) and physical model built in a powder-based system (c).

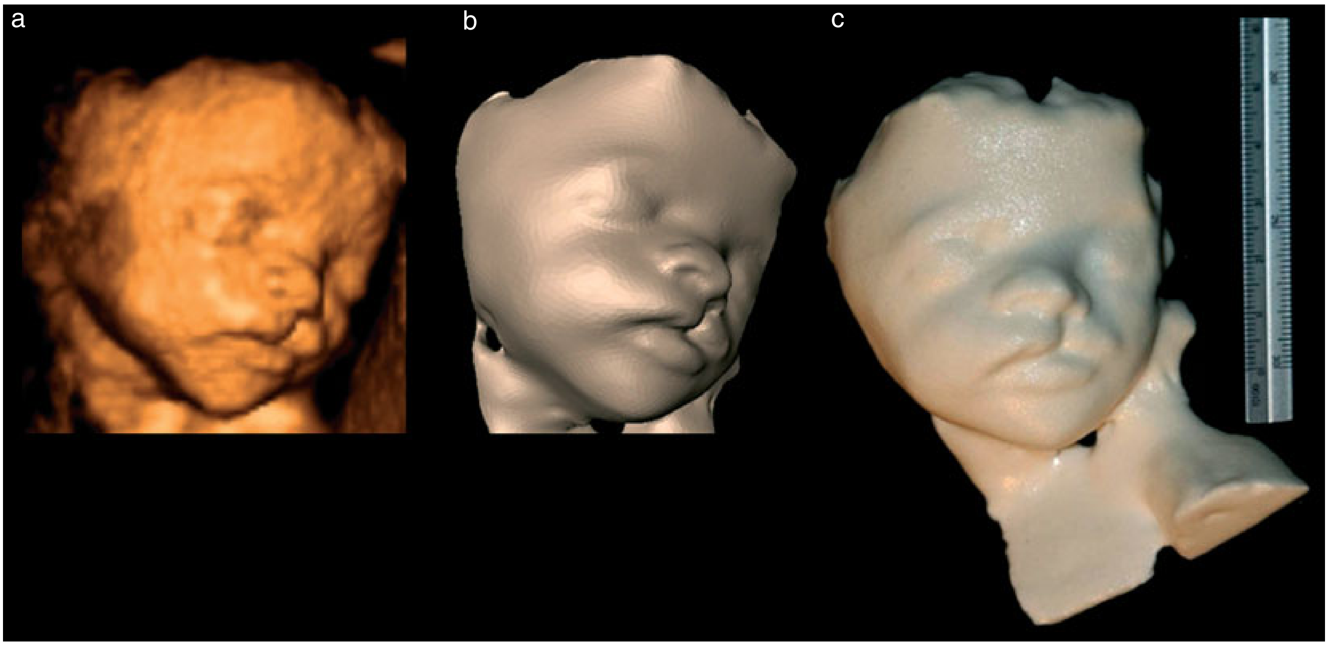

Figure 2 Fetus with a cleft lip at 28 weeks' gestation. Three-dimensional (3D) ultrasound image (a), 3D virtual model (b) and physical model built in a power-based system (c).

and the face from 3DUS (Figure 3). In case number 22, an achondroplastic dwarf at 34 weeks' gestation was evaluated by 3DUS, MRI and CT, all performed on the same day. The body was modeled using MR imaging, the face by 3DUS, and the skeleton using CT. Termination of pregnancy was carried out in the same week, and upon examination, the prototype and the fetus were found to be similar (Figure 4).

DISCUSSION

In this study the main outcomes were the possibility of creating 3D virtual models from 3DUS, MR or CT images both separately and also in various combinations. AM systems allow the conversion of a 3D virtual model to a physical model in a fast, easy and dimensionally accurate process[11,13,14]. The construction process transfers a 3D data file that specifies surfaces and solid internal structures to AM equipment that builds physical models through the superimposition of thin layers of raw materials[15]. This study introduced the use of AM models into fetal research, an area where studies on digital 3D modeling have been scarce. The results suggest a new possibility for interaction between parents and their unborn child during pregnancy, by physically recreating the interior of the womb during gestation, including physical appearance, actual size and malformations in some cases.

A key concern of this study was obtaining high-quality images that could be manipulated with 3D software without loss of accuracy[15]. Fetal movements during image acquisition are one of the principal difficulties. This is less of a problem with ultrasound as the real-time image can be frozen during a movement, unlike MR imaging. However the lower contrast resolution with 3DUS can cause difficulties at gray-scale boundaries. Image quality is directly associated with the precision of the final virtual 3D mathematical data that will be used to generate the prototype. Images from medical scans are acquired by 'slicing' the physical body. Superimposition of the captured slices from 3DUS, MRI or CT results in the construction of a virtual 3D computer-aided design (3D-CAD) model. The additive process begins when the virtual 3D-CAD model is sliced in layers that are used to guide the deposition of materials, layer by layer, to generate a physical 3D model[15,16].

Physical models have been used in fetal medicine for teaching purposes, but to the best of our knowledge no examples are known that apply contemporary physical modeling technology to their production[17,18]. Combining the different imaging modalities of 3DUS, MRI and CT may result in an increase in the interaction of both medical doctors and parents with the growing fetus, for educational and even future diagnostic purposes. Only two studies that use medical ultrasound scans and 3D models are currently available. Nelson and Bailey[18] converted 3DUS data to a set of polygons representing an isosurface that could be transferred to AM equipment to create a solid 3D object. This is considered the first attempt to transform fetal 3DUS data into AM physical models. The second project was developed by Blaas *et al.*[17], who calculated the volume of embryos and first-trimester fetuses by transforming the area of the embryo into a 3D virtual model.

Based on these experiments, our 3D fetal modeling began by using CT files to build physical models of fetal skeletons[15]. This study generated a series of bone connection structures in a 3D virtual environment. We used the design modeling software Autodesk Maya (Autodesk Inc., San Rafael, CA, USA) to keep the skeleton

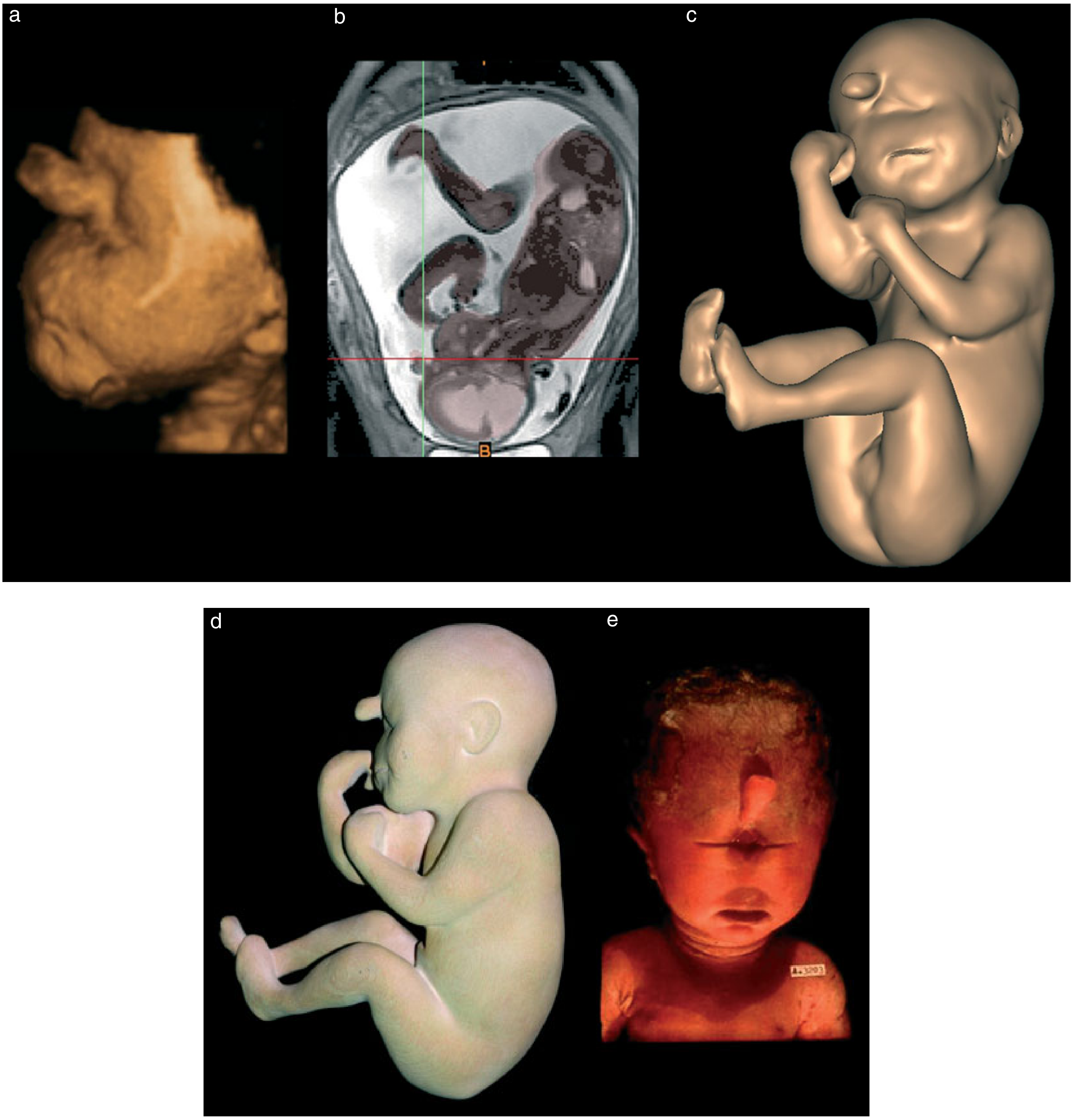

Figure 3 Fetus with alobar holoprosencephaly with a proboscis at 26 weeks' gestation. Three-dimensional (3D) ultrasound image (a), magnetic resonance image (b), mathematical 3D virtual model obtained from combined methods (c), physical model of the body built in a powder-based system (d) and photograph of the fetus (e).

whole, preserving its shape and spatial coordinates, and allowing the production of a physical model without losing accurate bond positioning. The next challenge was representing the body of the fetus as well as its external surface or skin, which was met by virtual separation of the CT slices. This interactive process visually detects the boundaries of the fetal body parts using a digital stylus pen that directly interacts with the computer screen. The resulting layers of the relevant fetal area were virtually overlapped, generating a 3D volumetric model.

Based on results from the CT files, MRI files were studied using the same manual segmentation techniques, in which every slice was virtually contoured and separated according to medical interpretation by a radiologist who assigned actual thicknesses to the MR scan. The main difference between CT and MR images was the quality of the contrast between the internal organs on the MR images. The high gray-scale contrast between internal regions allowed easier visual separation of the relevant areas using a liquid crystal display screen tablet. On CT scans, only the skeleton was easily identified. MRI

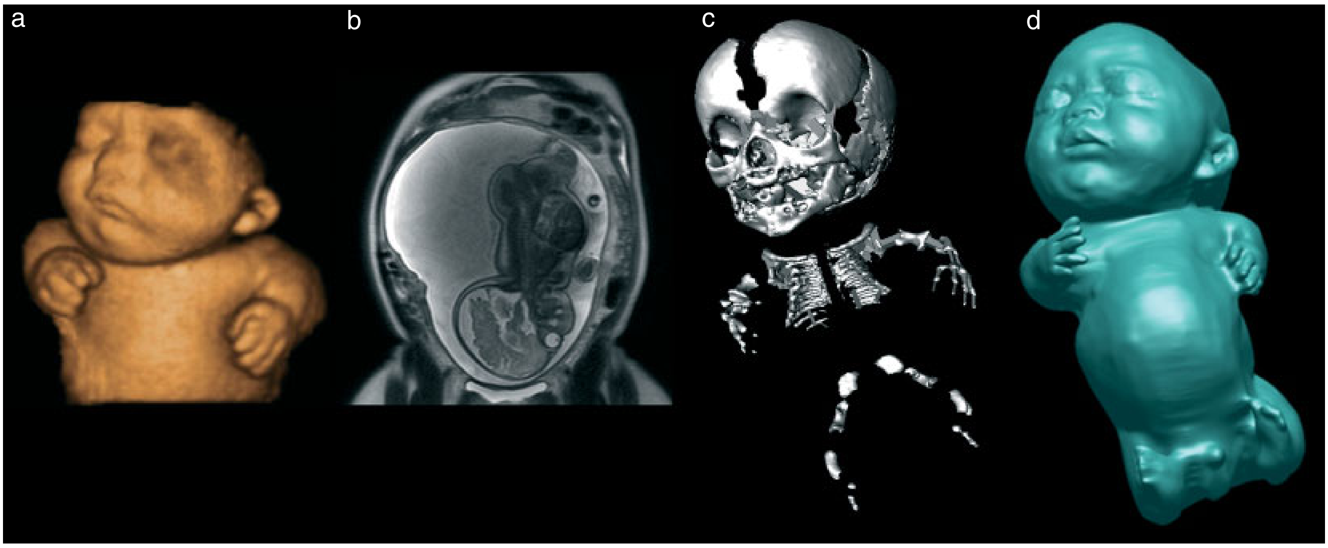

Figure 4 Fetus with achondroplasia dwarfism at 34 weeks' gestation. Three-dimensional (3D) ultrasound image (a), magnetic resonance image (MRI) (b), computed tomography (CT) image (c), mathematical 3D virtual model obtained from ultrasound and MRI (d), physical model built in photosensitive resin (e), skull model obtained from CT (f) and photograph of the fetus (g).

examinations are limited in their ability to provide numerous images with a high-quality outline. Image quality is best in the final stages of pregnancy, since the fetus has little space to move, and image quality is better if the fetus is immobile during the sweep[10]. The most substantial challenge in this study was the construction of models from 3DUS. This examination modality allows a faster sweep of the fetus, and the image is automatically transformed into 3D virtual images on the screen[19]. Depending on the size of the fetus, this process can permit the visualization of the complete body in the first trimester, or parts of the fetal body captured in separate sequences[20]. We used the tomographic ultrasound imaging function of the GE Medical Systems 4D View software to process the 3DUS images, and superimposed the results on MRI or CT files. The images obtained were exported to Mimics software for reconstruction of the 3D image, while maintaining accuracy and reliability. The protocols for the two preceding experiments were adopted for subsequent processing.

Using 3DUS, images from the entire gestation period could be captured for potential use with MRI and CT, including adding and combining features from these techniques. Since all 3DUS, MRI and CT files were obtained on the same day, detailed characteristics of the body could be combined, for example using 3DUS images for the face, hands or feet and MR images for the body, maintaining distances by obtaining several measurements by both technologies. The segmentation and reconstruction techniques developed for fetal modeling can be applied to the construction of both virtual 3D models and physical models, using the same data.

Regarding the production costs of the physical models, the two fabrication technologies adopted in these case studies are different and related to accuracy, materials and duration of construction, which are the main items to be considered in order to calculate costs. The Z Corporation technology (powder composite based mainly in plaster) is less accurate when compared to other AM technologies, but is also one of the fastest processes available on the market, and the physical models built through this process are less expensive, especially when compared to the stereolithography laser technology (liquid photo curable resin), which is one of the most accurate of existing techniques.

The techniques described in this study can be applied at different stages of pregnancy and constitute an innovative contribution to research on fetal abnormalities. We believe that physical models will help in the tactile and interactive study of complex abnormalities in multiple disciplines. They may also be useful for prospective parents because a 3D physical model with the characteristics of the fetus should allow a more direct emotional connection to their unborn child[3,21].

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