Published in final edited form as:

Phys Med Biol. 2011 August 07; 56(15): 4839–4879. doi:10.1088/0031-9155/56/15/014.

THE UF FAMILY OF HYBRID PHANTOMS OF THE DEVELOPING HUMAN FETUS FOR COMPUTATIONAL RADIATION DOSIMETRY

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Abstract

Historically, the development of computational phantoms for radiation dosimetry have primarily been directed at capturing and representing adult and pediatric anatomy, with less emphasis devoted to models of the human fetus. As concern grows over possible radiation-induced cancers from medical and non-medical exposures of the pregnant female, the need to better quantify fetal radiation doses, particularly at the organ-level, also increases. Studies such as the European Union's SOLO (Epidemiological Studies of Exposed Southern Urals Populations) hope to improve our understanding of cancer risks following chronic in-utero radiation exposure. For projects like SOLO, currently available fetal anatomic models do not provide sufficient anatomical detail for organ-level dose assessment. To address this need, two fetal hybrid computational phantoms were constructed using high-quality magnetic resonance imaging (MRI) and computed tomography (CT) image sets obtained for two well-preserved fetal specimens aged 11.5 and 21 weeks post-conception. Individual soft tissue organs, bone sites, and outer body contours were segmented from these images using *3D-DOCTOR*TM and then imported to the 3D modeling software package *Rhinoceros*TM for further modeling and conversion of soft tissue organs, certain bone sites, and outer body contours to deformable non-uniform rational B-spline (NURBS) surfaces. The two specimen-specific phantoms, along with a modified version of the 38-week UF hybrid newborn phantom, comprised a set of base phantoms from which a series of hybrid computational phantoms was derived for fetal ages 8, 10, 15, 20, 25, 30, 35 and 38 weeks post-conception. The methodology used to construct the series of phantoms accounted for the following age-dependent parameters: (1) variations in skeletal size and proportion, (2) bone-dependent

variations in relative levels of bone growth, (3) variations in individual organ masses and total fetal masses and (4) statistical percentile variations in skeletal size, individual organ masses, and total fetal masses. The resulting series of fetal hybrid computational phantoms is applicable to organ-level and bone-level internal and external radiation dosimetry for human fetuses of various ages and weight percentiles.

Keywords

NURBS; Fetus; hybrid phantom; radiation dosimetry; pregnant female

1. Introduction

The sensitivity of the developing fetus to ionizing radiation is a well-documented issue (ICRP, 2003). A number of deleterious health effects, including death, congenital malformations, mental retardation, and cancer, all demonstrate measurable correlations with both fetal absorbed dose and age. One versatile method to generate dose coefficients¹ for fetal exposures in medical imaging, as well as occupational or environmental scenarios, is through radiation transport simulation using computational phantoms of the pregnant female and her developing child.

Stylized versions of the human fetus have been developed previously by Stabin *et al* (1995) with subsequent organ refinements by Chen (2004) where fetal anatomy is modeled as an outer cylindrical shell of homogeneous fetal skeleton with hemispherical ends, and an inner volume filled with generic fetal soft tissue (see Figure 1A). Although used widely for reporting doses in diagnostic nuclear medicine (Russell *et al.*, 1997), this simplified treatment of the fetal anatomy does not permit detailed assessment of many fetal skeletal and tissue structures. In 2004, an image-based specimen-specific model of a 30-week human fetus, presented by Shi and Xu (2004), was constructed from segmented CT images obtained from an emergency scan of a pregnant female. Since the model was based on segmented *in vivo* CT images, it has greater anatomical accuracy as compared to previous stylized models, yet is still limited by image spatial resolution (see Figure 1B). The image slice thickness in this voxel model is 7 mm, a dimension quite large compared to anatomic dimensions of interest in fetal organ dose assessment. The limited spatial resolution of the images is manifest as its fetal skeleton lacks bone-specific detail. In addition, the CT scan of the pregnant female in the Shi and Xu (2004) model does not entirely encompass the fetal head, with the result being an incomplete model of the fetal cranium that had to be manually corrected. Additionally, skeleton-associated cartilage was not modeled by these investigators, again due to limitations of the *in vivo* maternal CT image.

Nevertheless, voxel models of the pregnant female can play an important role in verifying more approximate methods of fetal dose assessment in CT imaging. In 2008, Angel *et al* (2008) published a 24-patient retrospective study in which voxelized models of female abdominal anatomy were created covering a range of gestational ages of from 5 to 36 weeks

¹Defined as an organ absorbed dose per unit incident particle fluence (external exposures) or per unit radionuclide intake (internal exposures).

(see Figure 1C). Monte Carlo-based simulations of helical abdominal and pelvic CT scans were performed based on the General Electric series of multi-slice scanners. Fetal anatomy was differentiated only through a voxel-based separation of fetal bone (white) and soft tissue (red). Yellow pixels represent the amniotic cavity, while purple pixels represent the uterine wall. No differentiation of fetal organs were made. Whole fetal dose from abdominal and pelvic CT imaging were correlated to both maternal perimeter and fetal depth.

A third generation of anatomic computational model are hybrid phantoms in which organ boundaries and outer body contours are described by combinations of polygon mesh or NURBS (non-uniform rational B-spline) surfaces [see a review by Bolch *et al* (2010)]. In 2007, Xu *et al* (2007) published the first fully hybrid series of pregnant female models at gestational ages of 12, 24, and 36 weeks (see Figure 1D). The anatomic model of the fetus in the RPI series of pregnant female phantoms consists of a rescaled commercially available contour of the at-term newborn. Internal anatomy was limited only to a model of the fetal brain taken from the stylized model of Chen (2004) and the fetal skeletal model taken from the voxelized model constructed in Shi and Xu (2004). No further organs of fetal anatomy were implemented in this three-person pregnant female phantom series. In the study by Gu *et al* (2009), the 3-mo, 6-mo, and 9-mo hybrid phantoms of the pregnant female were used to assess organ doses to the mother, and to the fetal skeletal, brain, and whole body from CT imaging.

To date, anatomic models of the developing fetus have progressed in anatomical accuracy and flexibility, yet are still very limited in their definition of individual fetal organs and tissues. Even an organ as critical as the fetal skeleton is only approximately represented as shown in Figure 1B in the models of the RPI phantom series. Organ specific models of the developing fetus are important not only for prospective assessment of fetal cancer risk, but are vitally important in nuclear medicine dosimetry (following placental transfer) and in retrospective radiation epidemiology studies of specific cancers for *in utero* exposures. For later stages of pregnancy, and for higher weight percentile fetuses, radiation dose gradients will exist across the uterus during CT and fluoroscopic imaging, and organ-specific delineation in the fetal model becomes increasingly important. For radiation epidemiology studies, especially when considering bone-seeking radionuclides, the rather limited models of the fetal skeleton shown in Figures 1A to 1D do not permit a rigorous study of skeletal uptake and bone marrow dosimetry for correlations to observed cases of leukemia and bone cancer following in-utero exposure. To address these many limitations, a comprehensive imaging and modeling study was undertaken using high-resolution images of true fetal anatomy.

The true age of a fetus is typically a parameter that is not easily determined (ICRP, 2002) and is commonly reported in weeks from the last menstrual period (LMP) or weeks post-conception (PC). Conception is usually assumed to have occurred approximately two weeks after the last menstrual period (ICRP, 2002). Consequently, fetal ages reported in weeks LMP in the literature are converted to weeks PC by subtraction of two weeks (e.g., 40 weeks LMP is equivalent to 38 weeks PC). By definition, fetal age expressed in weeks PC represents the true age of the fetus and is, therefore, adopted throughout this document unless otherwise indicated.

2. Materials and Methods

2.1. Fetal anatomical specimens

Anatomic specimens for model creation were obtained from a well-preserved series of fetuses donated in the early 1960s to the University of Florida's Department of Anatomy and Cell Biology. Other than an approximate gestational age, no other documentation exists regarding their origin or donation history. Several specimens are accompanied by a label indicating an approximate gestational age. The entire collection includes specimens from approximately 10 to 30 weeks LMP. Desired specimens for potential model creation were chosen based on two criteria: (1) proximity to each of the ICRP reference ages and (2) external anatomy with no obvious physical deformities. Several specimens were imaged for future analysis. However, only two were used in the current study due to the time investment required to construct hybrid phantoms. After the two specimens were imaged, their ages were estimated using fetal biometry data to be 11.5 weeks and 21 weeks.

2.2. Imaging and aging of the fetal specimens

2.2.1. Imaging of the fetal specimens.—The 11.5 week and 21 week specimens were initially imaged at Shands Hospital, Gainesville FL using clinical magnetic resonance (MR) and computed tomography (CT). MR was chosen to emphasize the cartilaginous and soft-tissue anatomy while CT was chosen to capture the ossified bony regions. Image quality was acceptable in the case of the 21 week specimen but unacceptable in the case of the 11.5 week specimen. The soft tissue and undeveloped skeleton of the 11.5 week specimen were poorly visualized under CT and the small size of the fetus yielded MR image sets with high noise levels and insufficient in-plane resolution. This specimen was therefore re-imaged using high-field strength MRI at the Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) facility at the University of Florida.

Clinical MR scans were performed on a Siemens Magnetom Sonata superconducting MRI system with a 1.5 T static field strength, a maximal gradient amplitude of 40 mT m^{-1} , and a max gradient slew rate of $200 \text{ mT m}^{-1} \text{ s}^{-1}$. The fetal specimens were placed on the scan table oriented with the long axis of the body parallel to the scanner z-axis. A phased-array surface coil was used for signal reception. Three-plane localizer scans were performed followed by independent sagittal, axial and coronal localizer scans. High resolution T2 weighted images were then acquired using a 3D-FFT Fast Spin-Echo sequence with parameters as follows: TR of 2000 ms, TE of 190 ms, image matrix of 256×256 , 387 phase encoding steps, echo train length of 43, flip angle of 170° , pixel bandwidth of 200 Hz, slice thickness of 1 mm, and slice gap of 0 mm.

CT scans were performed on a Toshiba Aquilion multislice scanner (32, 64 slices). The fetal specimens were placed on the scan table oriented with the long axis of the body parallel to the scanner z-axis. CT topograms were acquired in the frontal and lateral projection for localization. Subsequently, a helical volume dataset was acquired with parameters as follows: 80 kVp, ~200–300 mA, scan FOV of 320 mm, reconstruction FOV of 250 mm, image matrix of 512×512 , slice thickness of 1 mm, and a slice gap of -0.5 mm ,

The 11.5 week specimen was also imaged under a standard spin-echo pulse sequence on a Bruker 4.7 T/200 MHz MRI spectrometer using the following scan parameters: T2 weighting, 33-cm bore, long axis of the body parallel to the z-axis, TR of 125 ms, TE of 5.3 ms, and a slice thickness of 0.35 mm.

Image sets were reviewed by co-author Dr. John Aris (UF Department of Anatomy and Cell Biology) to confirm the normality of each specimen's internal anatomy. Skeletal and soft tissues all appeared normal with the exception of the brain, which appeared to be underdeveloped within each specimen. This observation could indicate the presence of developmental abnormalities in all the imaged specimens or could be the result of brain tissue shrinkage due to extended formalin fixation (Quester and Schroder, 1997). Regardless of cause, this condition was easily corrected later during phantom development using established hybrid construction techniques.

2.2.2. Assessing the ages of the fetal specimens.—While the two fetal specimens have been previously distinguished by their estimated ages in order to provide a clear description of the image acquisitions, chronologically the age assessments did not occur until all CT and MR imaging had been completed. In order to estimate the ages of the two specimens, measured values of femur length and bi-parietal diameter were compared to the 50th percentile curves presented in Figs. 32 and 39 of Guihard-Costa and Larroche. Femur length and bi-parietal diameter measurements (39.7 mm and 58.7 mm, respectively) of the larger specimen yielded fetal ages of 20.5 and 21.5 weeks, respectively. The assigned age of the specimen was then given by their average – 21 weeks. Representative sagittal MR and CT images of this specimen are shown in Figures 2A and 2B, respectively. Femur length and bi-parietal diameter measurements (13.6 mm and 26.4 mm, respectively) of the smaller specimen yielded an age of 11.5 weeks. A representative sagittal NMR microscopy image of this specimen is shown in Figure 2C.

2.3. Construction of three base phantoms of fetal ages 11.5, 21, and 38 weeks

A considerable effort would be necessary to create a full series of hybrid fetal phantoms from specimens with ages corresponding to each fetal age of interest, specifically the ICRP reference fetal ages of 8, 10, 15, 20, 25, 30 and 38 weeks. As an alternative approach, the decision was made to construct the phantom series by systematically modifying and volumetrically rescaling three base phantoms: two constructed from the 11.5 week and 21 week imaged specimens, respectively, and one through modification of the existing 38 week at-term UF newborn phantom (Lee *et al.*, 2007; Lee *et al.*, 2010).

These three fetal ages roughly cover the early, middle and late stages of a typical human pregnancy, lending credence to adopting them as starting points for constructing phantoms at each fetal age of interest. The excellent image quality of the CT, MR, and NMR images of the 11.5 week and 21 week specimens indicated that hybrid base phantoms could be readily constructed for these two fetal ages using established techniques. A number of qualities made the UF hybrid newborn phantom an ideal candidate for constructing the third base phantom, including its age (38 weeks), the hybrid modeling techniques used in its construction, and its status as a completed member in the UF hybrid paediatric phantom

series. In particular, the NURBS-based anatomy easily permitted the necessary volumetric resizing and extremity repositioning.

All three base phantoms were constructed hermaphroditically to include both male and female reproductive systems. This design criterion limited the number of overall phantoms while still including male and female reproductive organs for relevant radiation dosimetry studies.

2.3.1. Segmentation of the 11.5 week and 21 week image sets.—A critical step in hybrid phantom construction is outlining or “segmenting” medical image sets in order to obtain three-dimensional representations of the relevant anatomy. Segmentation of the image sets of the 11.5 week and 21 week fetal specimens was performed using *3D-DOCTOR*TM (Able Software Corp., Lexington, MA), a 3D modeling and image processing software package. The images were imported into 3D-DOCTOR and the anatomical structures of interest were contoured manually using a combination of the computer mouse and a *Cintiq*TM (Wacom Co., Ltd.) tablet. A more detailed description of the entire segmentation process is provided in an electronic annex to this paper.

Once all the necessary contours had been completed, *3D-Doctor*’s complex surface rendering functions provided a polygon mesh model for each image set. Each polygon mesh model was exported as a *Wavefront Object* file, a format which preserves the position, dimension, and identity information of the segmented tissues and is easily imported into most 3D modeling software packages.

2.3.2. NURBS and polygon mesh modeling for the 11.5-week and 21-week phantoms.—Once image segmentation was completed, the polygon mesh *Wavefront Object* files were imported into *Rhinoceros*TM (McNeel North America, Seattle, WA), a NURBS and polygon mesh modeling software package. NURBS surfaces are a powerful modeling tool that allow for flexible, precise deformation of individual volumes, a useful feature particularly in regards to computational phantom construction. In constructing the 11.5 week and 21 week specimen-specific phantoms, *Rhinoceros* was used to a) correctly orient the polygon mesh models and b) incorporate NURBS surfaces into the phantom for various modeling requirements, including repair of segmentation artifacts, imparting deformability to certain structures, and adding skeletal cartilage and soft tissues that were not initially segmented. NURBS and polygon mesh modeling of the 11.5-week and 21-week specimen-specific phantoms represented the completion of two of the three base phantoms that were used to construct the completed fetal phantom series. Further details of the NURBS and polygon mesh modeling methodology is provided in an electronic annex to this paper.

2.3.3 Creating the 38-week base phantom.—The third and final base phantom used in development of the fetal hybrid phantom series was a modified version of the 38 week full-term UF hybrid newborn (Lee *et al.*, 2007; Lee *et al.*, 2010). This phantom required some simple modifications to make it consistent with the 11.5-week and 21-week specimen-specific phantoms, including (1) orienting the body to a fetal anatomical position, and (2)

homogenization of the differentiated skeleton. A detailed description of these modifications is provided in the paper's electronic annex.

2.4 Constructing the hybrid fetal phantom series

As previously mentioned, a series of hybrid fetal reference phantoms of 8, 10, 15, 20, 25, 30, 35 and 38 weeks, including the corresponding 10th, 50th and 90th weight percentiles, was constructed by volumetrically rescaling three base phantoms: two specimen-specific phantoms at 11.5 weeks and 21 weeks, and a modified version of the UF hybrid newborn at 38 weeks. With two exceptions, each base phantom was rescaled to a set of target gestational ages based on the proximity of the base phantom's age to the target ages. More specifically, the 11.5-week specimen-specific phantom was rescaled to 8 and 10 weeks, the 21-week specimen-specific phantom was rescaled to 15, 20, 25 and 30 weeks, and the 38-week modified hybrid newborn was scaled to 35 and 38 weeks. Although the 11.5-week specimen-specific phantom was closer in age to 15 weeks than the 21-week specimen-specific phantom, the latter was assigned because its more developed cranial plates better represented those of a 15-week fetus. Similarly, the 21-week specimen-specific phantom, and not the 38-week phantom, was scaled to 30 weeks because the latter contains secondary centers of ossification in the femur and tibia that are not yet developed at 30 weeks PC (Scheuer and Black, 2000).

Significant efforts were directed to the following age-dependent areas to ensure the series of scaled phantoms properly represented the target gestational ages: (1) bone site-specific levels of ossification, (2) densities of homogeneous fetal bone, (3) overall skeletal size and proportion, (4) individual soft tissue organ masses and (5) total body mass. With one exception, all members of the series were constructed using the same general procedure. Due to the rapid physical development that occurs during the embryonic stage, the 8 week phantom was constructed using a separate procedure that accounted for the substantial morphological changes observed during the transition period from embryo to fetus.

2.4.1 Age-dependent homogeneous bone volume fractions (HBVF).—Simple volumetric scaling of a base phantom to a target gestational age – by matching a given target biometric parameter, for example – would fail to properly account for the relative changes in skeletal ossification in transitioning from one fetal age to another. For example, the femur of a 30-week fetus contains proportionally more ossified bone than is seen at 21 weeks. The phantom construction process presented in this study addresses this issue by systematically altering, by fetal age, the relative levels of ossification of the majority of bone sites for each individual phantom. Targeted relative amounts of ossification were approximated by deriving a set of age-dependent, bone site-dependent homogeneous bone volume fractions (HBVF), defined mathematically for an individual bone site as the volume ratio of ossified bone to total bone (ossified bone plus unossified cartilage/connective tissue). For each targeted gestational age, these HBVFs were incorporated into the skeleton of the corresponding base phantom, a process which yielded, in each instance, a new, modified base phantom whose skeleton better represented that of the targeted fetal age. For example, incorporating 30-week HBVFs into the 21-week specimen-specific phantom created an undersized 30-week phantom which was later resized to create a 30-week phantom of the

correct overall size as well as of the appropriate levels of skeletal ossification. This process was performed for each target fetal age/base phantom combination between 10 weeks and 38 weeks, yielding seven modified base phantoms. Table 1 summarizes the final set of target HBVF values. Details regarding the derivation and implementation of the HBVFs are provided in the electronic annex to this paper. A separate scaling process was employed at 8 weeks (see below).

2.4.2. Age-dependent homogeneous fetal bone densities.—Appropriate mass densities were required to estimate the masses of each phantom's homogeneous bone volumes. Human fetal bone densities are relatively unknown. ICRU Report 46 reports limited density data, specifically, cortical bone densities for 20 weeks LMP and 30 weeks LMP and a whole femur density for 20 weeks LMP (ICRU, 1992). A basic approach was therefore adopted to approximate the homogeneous bone densities of the fetal skeleton. It is well documented that the cranium of the human embryo develops primarily by membranous ossification while the remaining skeleton develops by a mixture of enchondral and membranous ossification (Oestreich, 2007). This explains why the newborn homogeneous bone densities reported by Pafundi *et al* showed a notable difference between the whole cranium ($1.46 \text{ g}\cdot\text{cm}^{-3}$) and the remainder of the skeleton ($\sim 1.33 \text{ g}\cdot\text{cm}^{-3}$) (Pafundi *et al.*, 2009). Based on these observations, a basic approach was adopted to estimate fetal homogeneous bone densities: two sets of age-dependent fetal homogeneous bone densities were derived by linearly interpolating between the ICRU 46 cartilage density ($1.1 \text{ g}\cdot\text{cm}^{-3}$) at 8 weeks and the cranium and lumbar vertebra homogeneous bone densities reported by Pafundi *et al* at 38 weeks ($1.46 \text{ g}\cdot\text{cm}^{-3}$ and $1.37 \text{ g}\cdot\text{cm}^{-3}$, respectively). In this case, the lumbar vertebra served as a density surrogate for non-cranial bones of the skeleton. ICRU 46 cartilage density was assumed at 8 weeks as this is the timeframe in which the majority of bone sites begin to ossify (Scheuer and Black, 2000).

2.4.3 50th percentile phantoms for 10 weeks and older – Volumetric scaling by femur length and bi-parietal diameter.—As discussed previously, implementation of the target HBVF data in the base phantoms yielded seven new, HBVF-modified base phantoms, each with skeletal anatomy that better represented their associated target fetal ages. However, while the HBVF adjustments provided corrections to the relative levels of ossification of the fetal skeleton, they did not address differences in the absolute skeletal size. These skeletal size differences were accounted for by volumetrically scaling base phantoms to targeted values of femur length and bi-parietal diameter taken from Figures 32 and 39 of Guihard-Costa and Larroche (1995). Table 2 summarizes the femur lengths and bi-parietal diameters adopted as target values from this 1995 study. These two biometrical parameters were chosen based on two criteria: (1) for a given target fetal age, they provide a mechanism for approximating the absolute size of the skeleton and (2) they account for age-dependent proportion variations between the skull and other bones of the skeleton.

Total fetal body weight is an additional parameter reported by Guihard-Costa and Larroche (1995). In addition, percentile curves are presented for all three biometrical parameters. The percentile data permitted the current study to construct a reference fetal phantom series that accounted for the size variations among fetuses of the same gestational age. The graph of

fetal body weight in Figure 2b of Guihard-Costa and Larroche (1995) shows a diminishing spread of weights with decreasing gestational age, particularly near 16–17 weeks LMP (the age scale used in this study). These observations prompted the decision to construct only single, 50th percentile phantoms for targeted fetal ages 15 weeks and younger, and 10th, 50th, and 90th percentile phantoms for gestational ages 20 weeks and older (10th and 90th percentile phantom construction is discussed below). The seven HBVF-modified phantoms at 10, 15, 20, 25, 30, 35, and 38 weeks were thus scaled in two steps to yield seven new, biometry-scaled 50th percentile phantoms. First, each HBVF-modified phantom was volumetrically scaled in its entirety to match the targeted 50th percentile femur length. Second, the head – including all skeletal and soft tissue anatomy contained within – was volumetrically scaled to match the target 50th percentile bi-parietal diameter. Various tools in *Rhinoceros™* were used to assess femur lengths and bi-parietal diameters in ways that closely mimicked standard ultrasonography measurement practices (Seeds, 1996). The details of how the measurements were obtained are provided in our electronic annex.

2.4.4 50th percentile phantoms for 10 weeks and older – Matching individual organ masses and total mass.—In order to provide the most complete representation of the fetal anatomy, the individual organ masses and total fetal masses of the 50th percentile biometry-scaled phantoms needed to be adjusted to appropriately representative values. Target organ and total masses were obtained from three literature sources. The first is the study by Archie et al (2006) in which regression curves are compiled, with standard deviations, for the masses of major soft tissue organs obtained from a variety of fresh autopsy studies performed by several authors. The second study was that of Guihard-Costa et al (2002) who reported total fetal weight, with percentiles, obtained from fresh autopsy of 476 normal fetuses. Finally, ICRP Publication 89 (ICRP, 2002) was consulted in which detailed 50th percentile anatomical and physiological data for a number of postnatal ages is reported, beginning with the newborn.

The individual fetal soft tissue organ masses reported by Archie *et al* were adopted as target values for 50th percentiles between ages 10 weeks and 38 weeks. Specific soft tissue organs include brain, thymus, lungs, heart, liver, spleen, adrenals, pancreas and kidneys. Archie *et al* did not report pancreas masses below 17 weeks (19 weeks LMP). Target pancreas masses were derived for 10 and 15 weeks by averaging the pancreas-to-liver mass ratios (0.0275) of the target fetal ages between 20 and 38 weeks and multiplying by the target liver masses for those ages. Fetal thyroid masses were also not reported by Archie *et al* and so ICRP Publication 89 reference thyroid masses were adopted for 50th percentile phantoms between the ages of 10 and 38 weeks. Target total fetal masses for all ages and percentiles were obtained from Figure 2b of Guihard-Costa *et al* (1995), which graphically presents mean fetal weight and various weight percentiles as a function of gestational age. Values were read directly from the figure.

The UF hybrid newborn contains a large number of individually defined anatomical structures. Apart from homogenization of the skeleton, the 38 week base phantom and its derived phantoms contained all the anatomical structures originally defined in the UF hybrid newborn, even those structures were not modeled in the 11.5 week and 21 week specimen-

specific phantoms. Any structure in any phantom that did not have a target value assigned to it was left unaltered following biometrical scaling.

All soft tissue mass densities, with the exception of the walls of gastrointestinal system, were obtained from ICRU Report 46 (ICRU, 1992). The mass density of the walls of the gastrointestinal system was obtained from ICRP Publication 89 (ICRP, 2002).

Individual soft tissue organs with target masses were resized by adjusting their NURBS surface contours and, hence, their individual volumes. A combination of *RhinocerosTM* tools were used to alter individual NURBS surfaces, including the careful manipulation of NURBS control points, *3D Scale* and *Surface Offset*. Care was taken to maintain the original organ morphologies, orientations, and locations as observed in the base phantoms.

“Empty” volumes within the NURBS outer body contour that were not explicitly defined by a polygon mesh or NURBS surface was declared residual soft tissue (RST). Targeted values of total fetal mass were then matched by altering the control points of the outer body contour until a target *total* volume was met. Target total volume was derived by solving for the mass of RST that would have to be summed with the masses of the explicitly defined anatomy to yield the target total mass. The morphological adjustments made to the outer body contour were limited to the torso and extremities. The outer contours around the skull and near the spine were left unaltered.

2.4.5 10th and 90th percentile phantoms for 20 weeks and older.—As previously discussed, the decision was made to construct 10th and 90th percentile phantoms at 20 weeks and above. These phantoms were generated in a manner similar to the 50th percentile phantoms, including biometry scaling using femur length and bi-parietal diameter as well as matching individual soft tissue organ masses and overall total masses. However, the 10th and 90th percentile phantoms were not biometry-scaled from the HBVF-modified phantoms like the 50th percentile phantoms but rather from the completed 50th percentile phantoms themselves. The purpose of this variation in the biometry scaling methodology of the 10th and 90th percentile phantoms is purely for design convenience and time efficiency; for a given target fetal age organ masses, locations and proportions of completed 50th percentile phantoms are more physically accordant with their 10th and 90th percentile counterparts than their HBVF-modified phantom counterparts, a fortuity which minimizes design effort in creating 10th and 90th percentile phantoms. This design approach causes the 10th, 50th and 90th percentile phantoms for a given age to have identical levels of skeletal ossification in each bone site and similar soft tissue organ locations and proportions.

With the exception of the thyroid, the same set of soft tissue organs that were targeted for specific masses in the 50th percentile phantoms were also targeted to specific masses in the 10th and 90th percentile phantoms. Mean masses and standard deviations reported in Archie *et al* were used to derive 10th and 90th percentile masses between the ages of 20 and 38 weeks. As previously discussed, Archie *et al* did not report mass data on the fetal thyroid. In addition, ICRP Publication 89 reported only 50th percentile fetal thyroid masses. Consequently, for 10th and 90th percentile phantoms, thyroid masses were left unaltered after volumetric scaling of the 50th percentile reference phantoms to the two other percentiles.

The same approach was adopted for those remaining soft tissue organs which had no specific target mass. As with the 50th percentile phantoms, target total fetal masses were obtained from Figure 2b of Guihard-Costa *et al* (1995).

2.4.6 The 8-week 50th percentile phantom.—The 8th week of intra-uterine life measured from the point of conception corresponds roughly to the end of the embryonic phase of development and is a period of significant morphological changes within the growing human. The work of Bradley Smith and the Multi-Dimensional Human Embryo project visually captures these morphological changes that occur throughout the embryonic period with traditional photography and high-field strength NMR microscopy imaging. For this project, T1-weighted NMR images of a Carnegie Stage 23 human embryo aged approximately 56 days post-ovulation (8 weeks) was kindly provided to us by Dr. Smith. Major soft tissue organs (except the thyroid due to its size and/or limited image contrast) and outer body contour of this embryo were segmented and used to evaluate a biometrically-scaled version of the completed 10 week 50th percentile phantom. The scaling was based solely on the 50th percentile bi-parietal diameter reported by Guihard-Costa *et al* for 10 weeks LMP. Femur length was not included as a scaling parameter since data for 10 weeks LMP were not reported in that study. The segmented images of the Stage 23 embryo showed that the biometrically-scaled 8-week phantom failed to correctly represent the morphology of an 8-week embryo, particularly in regards to organ masses and the morphometry of the extremities.

Comparisons of the masses of the segmented organs with ICRP Publication 89 reference 8-week organ masses showed that the two data sources were generally in disagreement, particularly in regards to the brain mass. In addition, several organs scaled to ICRP Publication 89 reference masses showed severe disparities in size proportions with the overall size of the segmented embryo. Comparisons could not be made with Archie *et al* as organ mass data below 10 weeks were not reported in that study.

The limited biometry measurements and organ mass data for 8-weeks rendered insufficient the phantom scaling methodology applied to the later fetal ages. The decision was thus made to create a 50th percentile 8-week phantom based on the organ volumes, total volume and overall morphometry of the segmented images of the Stage 23 embryo. First, the completed 50th percentile 10-week phantom was volumetrically downscaled based on the segmented brain volume since that organ greatly influences overall body size at that age. Per the discussion in Section 2.4.1, the entire skeleton was assumed to be completely cartilaginous at 8 weeks and, therefore, the ossified portions of skeleton, which originated from the 10-week phantom, were retagged as cartilage with an ICRU 46 density of 1.1 g-cm⁻³. Measurements of the crown-rump length (CRL) and the lengths of the extremities showed the scaled phantom over-estimated these parameters by approximately 8% and 55%, respectively. The extremities were shortened using the *ID Scale* command along the long axes of the upper and lower portions of the limbs, e.g. between the shoulder and elbow and between the elbow and wrist. Using the *ID Scale* command the CRL was reduced by scaling the torso and extremities along the CRL axis. The individual organ volumes were matched to the segmented volumes within 1% with care taken to incorporate the locations and morphometries of individual organs. Due to its small size and/or limited image contrast in

that region of the body, the thyroid could not be identified and segmented. The ICRP 89 reference thyroid mass appeared grossly oversized compared to the rest of the body when a scaled version of the 11.5 week thyroid was inserted. Consequently, the 8-week fetal thyroid was modeled by adopting a downscaled version of the 10-week 50th percentile thyroid. The magnitude of the rescaling was equivalent to downscaling the brain from 10-week 50th percentile to the target 8-week segmented value. The total volume of the phantom was matched to the total volume encompassed by the segmented outer body contour of the Stage 23 embryo. Appropriate mass densities were adopted as necessary.

3. Results and Discussion

3.1. 11.5 week and 21 week specimen-specific base phantoms

Figures 3A and 3B graphically illustrate the completed 11.5 week and 21 week specimen-specific base phantoms, respectively. In particular, the figures demonstrate the ability of the hybrid construction process to accurately capture fetal anatomy from medical image sets of sufficient image quality. Figures 4A and 4B display the skulls of the 11.5 week and 21 week specimen-specific base phantoms, respectively. The immature facial bones, cranial plates and mandible of the 11.5-week specimen are well delineated in the upper panel of Figure 4. The gaps among the fibrous tissues surrounding the cranial plates and facial bones are a consequence of limited image contrast and the spatial separation of the underdeveloped regions of ossification, meaning manual insertion of fibrous tissues into the gaps could not easily have been performed. Conversely, the more physically mature cranium of the 21-week specimen provided a better template from which to approximate the locations of fontanels and other fibrous tissues. Thus, within the cranium of the 21-week specimen-specific phantom, efforts were taken to construct gap-free interfaces between homogeneous bone and fibrous tissues, including all fontanels, the orbits of the eyes, nasal regions, and the basicranium. Figure 5 shows the 21-week specimen-specific spine and sacrum. A volumetrically downscaled version of the cartilage NURBS surfaces of these structures was incorporated into the 11.5 week specimen-specific phantom. The figure shows the anatomical morphology of the bony regions of the spine and sacrum were sufficiently captured by the medical image sets and subsequent segmentation. The artistically designed cartilage NURBS surfaces sufficiently represent the morphology of the sacrum and the cervical, thoracic and lumbar regions of the spine. The ability to acquire high-quality medical images of *in vivo* fetal anatomy from preserved specimens and apply established hybrid phantom construction methodologies has produced, in this case, two specimen-specific hybrid phantoms that, when combined with an appropriately modified 38-week fetal phantom, constitute a set of base phantoms from which to construct a more complete family of fetal models.

3.2 Age-dependent homogeneous bone volume fractions (HBVF)

The homogeneous bone volume fractions derived using the methodology presented above provide, at a minimum, a systematic, internally consistent treatment of the age-dependent changes in fetal skeletal ossification. However, a strong claim cannot be made that the HBVFs derived in this study truly quantitatively represent the increasing levels of skeletal ossification as a function of age. Although the derivations incorporate “known” data points

obtained from the 11.5 week and 21 week specimen-specific phantoms, even these data are highly dependent primarily on the specimens themselves and secondarily on the segmentation and modeling techniques of the authors. Data obtained from the UF hybrid newborn and incorporated at 38 weeks are limited by the modeling of the bone sites of that phantom. The skeletal cartilage/connective tissue in that case was applied as a single uniform layer over all ossified regions bone with a thickness that was calculated to match the total cartilage mass with the ICRP 89 reference value. This simplistic treatment of the unossified regions of the bones of the newborn skeleton yields homogeneous bone volume fractions which may be highly approximate in nature. The assumption that all bone sites in the skeleton are completely unossified at 8 weeks is generally appropriate for all bone sites except the clavicle, which can begin ossifying weeks earlier. Since the amount of ossification of the clavicle at 8 weeks can be expected to be low, the decision was made to anchor the clavicle HBVF to a null value at 8 weeks to retain consistency with the rest of its skeleton. The paucity of data related to this particular aspect of fetal development suggests the need for further study on a much larger sample of fetal specimens. Obvious limitations notwithstanding, the HBVFs were implemented into the fetal phantom series using a methodology which roughly mimicked known ossification patterns of the skeleton. This is perhaps best illustrated in Figure 6, which shows the increasing levels of ossification of the os coxae of the 20, 25 and 30 weeks phantoms, particularly the appearance of a new primary center of ossification in the pubis. The same level of modeling detail was applied to all bone sites adjusted for age-dependent HBVF.

3.3 Age-dependent homogeneous fetal bone densities

Fetal homogeneous bone densities were derived by linearly interpolating between known newborn cadaver data obtained from Pafundi *et al* (2009) at 38 weeks and assuming ICRU 46 reference cartilage density at 8 weeks. Pafundi *et al* reported homogeneous bone densities for multiple bone sites and, therefore, age-dependent densities could have been derived for each individual bone site. However, because the whole bone homogeneous bone densities of the non-cranial bones exhibited little variation, the lumbar vertebra homogeneous bone density was adopted as a surrogate for all non-cranial bones at 38 weeks. The homogeneous bone density of the cranium was left separate as its value was slightly higher compared to the average homogeneous bone density of all non-cranial bone sites. The rationale for the separation of the cranium from the rest of the skeleton was introduced previously and is related to the differing routes of bone ossification for the two groups of bones. A rough verification was performed on the adoption of linearly interpolated lumbar vertebra homogeneous bone densities as surrogates for non-cranial bones. ICRU Report 46 reports a whole-bone homogeneous femur density of 1.12 g-cm^{-3} for 20 weeks LMP. Using the cartilage and homogeneous bone volumes of the 21-week specimen-specific femur (corrected for ossification using the derived HBVF curves) and the ICRU Report 46 whole femur density, a homogeneous bone density was approximated at 1.16 g-cm^{-3} . The 18-week homogeneous bone density obtained from the linearly interpolated lumbar vertebra data was approximate 1.19 g-cm^{-3} , a difference of less than 3%. Admittedly, this type of verification is rough at best. However, it does provide some indication that adopting the derived homogeneous bone densities is reasonable.

3.4. Target organ masses and total masses

The post-natal pediatric hybrid phantoms constructed previously at the University of Florida were specifically designed to target the ICRP reference individuals at ages of 0, 1, 5, 10, and 15 years of age, with heights, weights, and organ masses taken from ICRP Publication 89 (ICRP, 2002). That ICRP publication additionally reports reference masses for fetal organs at eight fetal ages – 8, 10, 15, 20, 25, 30, 35, and 38 weeks – all of which were targeted in this study. Nevertheless, a secondary goal of the study was to explore models at their 10th and 90th percentiles at each fetal age, and thus it was necessary to adopt target mass values that were accompanied by statistical percentile values. The means and standard deviations reported by Archie *et al* (2006) fulfilled this requirement as it provided statistically strong regression curves derived from a multiple cadaver studies performed by independent authors. The means of organ masses were comparable at all reported ages except, notably, the brain at 10 weeks. ICRP 89 reports a brain mass twice that given in Archie *et al* at that age (6.7 g vs. 3.2 g). The Archie *et al* brain mass at 10 weeks (12 weeks LMP) is solely determined by the data reported by Hanson *et al* (2003) on a cadaver sample size of n=6. The ICRP 89 reference brain mass at 10 weeks (12 weeks LMP) is determined by the fresh brain mass data reported by Guihard-Costa *et al* (Guihard-Costa *et al.*, 2002) which contains no sample points at 12 weeks LMP. In addition to the statistical advantage, the Archie *et al* 10-week brain mass fits well into the cranial vault of the 10-week phantom. Given the proximity of the ages of the 10-week phantom and the 11.5-week base phantom, the volume of the cranial vault of the former is likely well representative of that age. This observation lends further credence to adopting the brain mass reported by Archie *et al* at 10 weeks and, perhaps, helps confirm the validity of adopting the Archie *et al* data where possible for the remaining organs and target fetal ages.

Unlike that given in ICRP Publication 89, Archie *et al* (2006) did not report organ masses for 8 weeks. ICRP 89 data were consequently compared to segmented image data obtained from the 8-week embryo. They were found to be divergent particularly with respect to the brain (3.9 g vs. 0.7 g) and pancreas (0.39 g vs. 4.07×10^{-4} g). Consequently, the segmented organ volumes of the 8 week embryo were adopted as targets in lieu of the ICRP 89 masses reported at 8 weeks (see Table 6 and its footnotes for further details).

For the following reasons, targeted values for total fetal masses were adopted from the study of Guihard-Costa *et al* (1995) rather than from values given in either ICRP Publication 89 (ICRP, 2002) or Archie *et al* (2006). As with reference organ masses, ICRP 89 does not report statistical spreads or percentiles for total fetal mass. While Archie *et al* (2006) does report age-dependent total fetal mass and its standard deviation, the data of Guihard-Costa *et al* (1995) was preferred for internal consistency with its data on femur length and bi-parietal data – values adopted earlier for adjustment of overall fetal size.

The mass data of the 50th, 10th, and 90th percentile phantoms are presented in Tables 3, 4 and 5 respectively, including, where appropriate, the actual mass of each anatomical structure, its target mass, and the percent difference between the two. In Table 6, the ‘Target Mass Comments’ column provides a numerical keys to descriptions of the status of the masses of each anatomical structure at the culmination of the phantom construction process (e.g., whether a structure has a final mass that is a result of the various stages of volumetric

scaling or targeted from data in the literature). Masses with target values were matched to within 1%.

It is important to note that although the masses reported in Tables 3, 4 and 5 were calculated using volumes obtained directly from *Rhinoceros*TM, these values may not be identical to the masses calculated after voxelization, a process generally required to convert hybrid phantoms into a format useable in current radiation transport codes (Lee *et al.*, 2007; Lee *et al.*, 2010).² By its nature, the voxelization process removes any partially-overlapping volumes within a phantom, resulting in possible disparities with the masses calculated from volumes obtained in *Rhinoceros*TM. While much effort was taken to minimize or account for possible overlapping structures within each fetal hybrid phantom, the close proximity of multiple complexly-shaped structures, particularly within the bones of the skeleton, make detecting all overlapping structures before voxelization occurs a nearly impossible process.

The percent differences between total fetal mass and target total fetal mass exhibit a notable trend: base phantoms that were scaled to older ages tended to be on the *underweight* side of the percent difference and base phantoms that were scaled to younger ages tended to be *overweight* side of the percent difference. Bernstein et al (1997) propose the addition of subcutaneous fat within the fetal body can be described by a 2nd order quadratic function that accelerates with increasing gestational age. These findings could explain the systematic need to manually increase the amount of adipose tissue when scaling to older fetal ages and to remove excess adipose tissue when scaling to younger gestational ages. Note that no such trends were noticed among the three weight percentiles within a given fetal age. This may indicate that differences in total mass among fetuses of the same age are more a function of overall skeletal size and development rather than variable rates of subcutaneous fat accumulation.

The soft tissue densities of the hybrid phantoms were primarily adopted from ICRU Report 46, which gives data for a wide range of anatomical structures. In some cases, fetal values are reported and were thus adopted here. In cases where fetal values are not reported, suitable surrogates were adopted. The ‘Density’ column of Tables 3, 4 and 5 list the specific soft tissue densities assumed in model creation. Specific ICRU Report 46 entries for each tissue density are listed under the ‘Density Comment’ column of Table 6.

Figure 7 provides left sagittal views of the entire family of fetal hybrid phantoms constructed by the methods presented in this study. The individual fetuses are to-scale relative to one another. The outer skin contour is depicted in translucent dark grey, homogeneous bone is depicted in red, and the soft tissue organs are presented in a variety of distinguishing colors. The position of the extremities in the UF fetal model series of Figure 7, while reasonably representative of in-utero posture, are approximated for the two oldest ages, and were left as imaged for the 11.5 and 21 week base phantoms and their scaled counterparts. As discussed in Section 2.3.3, however, the extremity positions can be easily reconfigured as desired or necessary for dose assessment.

²As noted in Kim et al. (2011), however, progress has recently been made on the direct use of NURBS/PM-based phantoms within the radiation transport code GEANT4.

4. Conclusions

The series of fetal hybrid phantoms developed in this study represents an eighteen-member addition to the existing UF family of post-natal hybrid computational phantoms and spans fetal ages of 8, 10, 15, 20, 25, 30, 35 and 38 weeks, including 50th weight percentiles at all ages and 10th and 90th weight percentiles at 20 weeks and older. Two specimen-specific phantoms of fetuses aged 11.5 weeks and 21 weeks were constructed using established hybrid phantom construction techniques (Lee *et al.*, 2007; Lee *et al.*, 2010), including segmentation of medical images obtained of *in vivo* anatomy and conversion of segmented anatomy to polygon mesh objects and NURBS surfaces for more detailed 3D modeling of the soft tissue organs and skeleton. The 38-week UF hybrid newborn was repositioned into a fetal position and internally modified to make it consistent with the two younger specimen-specific phantoms. Together these three phantoms constituted a set of base phantoms which was used to derive the complete fetal phantom series using a detailed methodology which systematically accounted for (1) changes in absolute skeletal size and relative proportions through the use of femur length and bi-parietal diameter biometry data (Guihard-Costa *et al.*, 1995), (2) changes in the relative levels of bone growth (ossification) through the derivation and incorporation of age-dependent, bone-dependent homogeneous bone volume fractions and (3) age-dependent changes in individual soft tissue organ masses and total fetal masses (Archie *et al.*, 2006; ICRP, 2002). Individual organs and total masses with target values were matched to within a difference of 1%.

The hybrid fetal phantoms developed in this study represent a significant advancement over currently available models in three distinct areas: (1) the detailed treatment of all major soft tissue organs and the developing skeleton, including both ossified homogeneous bone and unossified cartilage for each major bone site, (2) a finer grid of fetal ages (8 in total) spanning nearly the entire extent of a typical human pregnancy- from the end of the embryonic period to full-term, and (3) the consideration of different statistical percentiles within a given fetal age for (a) the fetal skeleton (via femur length and bi-parietal diameter), (b) individual organs masses and (c) total fetal mass. Current efforts are now devoted to developing a complimentary series of pregnant female phantoms using the fetal models presented in this study, with applications to fetal dosimetry in both environmental exposures and medical imaging of the mother. Furthermore, estimates of bone-specific marrow mass in the UF fetal phantom series require additional information on the marrow and mineral bone volume fractions of fetal spongiosa, and this data is being sought through further NMR microscopy imaging.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This work was supported in part by Grants FI6R-516478 (SOUL Project) and FP7- 249675 (SOLO Project) from the European Union with the University of Florida. The authors wish to extend their sincere appreciation to Dr. Moira R. Jackson, Director of the State of Florida Anatomical Board, and to Dr. William A. Dunn, Jr., Chair of the UF Department of Anatomy and Cell Biology, for their permission to access the fetal specimen collection for imaging. Thanks are also extended to Dr. Glenn Walter (Director) and Sean Germain (Staff Scientist) of the UF

Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) Facility of the UF McKnight Brain Institute for use of the 4.7 T spectrometer. Finally, the authors extend their appreciation Cassandra Lucio of the University of Florida's Department of Anthropology for her knowledge and guidance on topics of human skeletal development, and Dr. Choonsik Lee of the National Cancer Institute for his review of the final manuscript.

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Figure 1.

Graphical survey of previously published fetal computational phantoms: (A) Stylized model of the 36-week fetus from Stabin et al.; (B) Voxel model of the 30-week fetus from Shi and Xu (2004); (C) Hybrid model of the 24-week fetus from Xu et al. (2007); and (D) Voxel model of a 35-week fetus from the 24-patient study by Angel et al. (2008).

Figure 2. Representative images used to construct specimen-specific models: (A) 1.5 T sagittal MR image of the 21-week fetus, (B) transverse CT image of the 21-week fetus, (C) 4.7 T NMR microscopy image of the 11.5-week fetus. (D) 4.7 T NMR microscopy image of the 11.5-week fetus showing image artifacts.

Figure 3. NURBS-based anatomic models of the (A) 11.5 week and (B) 21 week fetus. Images for each include a view of internal organs with (left) and without (center) transparent outer body contour, and with the skeleton removed (right). In the skeleton, red indicates ossified trabecular spongiosa and gray indicated unossified bone.

Figure 4.
Images of the mandible and cranial plates within the (A) 11.5 week and (B) 21 week fetal hybrid phantom.

Figure 5.
(A) Sagittal and (B) oblique view of the spine and sacrum of the 21-week fetal model.

Figure 6.
Representative images of the hybrid models of the os coxae at gestational ages of 20, 25, and 30 weeks.

Figure 7.

Left lateral views of the UF series of fetal hybrid phantoms at three different weight percentiles and eight different gestational ages. All images – excluding the inserted images of the 8 and 10 week fetus – are to relative scale.

Derived homogeneous bone volume fractions as a function of bone site and gestational age. Bolded values indicate data obtained from constructed hybrid phantoms or from modeling assumptions.

Table 1.

Gestational age		HBVF														
(weeks PC)	Cranium	Mandible	CV	TV	LV	Sacrum	Scapula	Pelvis	Clavicle	Ribs	Humerus	Radius	Ulna	Femur	Tibia	Fibula
8	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
10	0.03	0.24	0.05	0.04	0.05	0.03	0.31	0.13	0.28	0.13	0.20	0.33	0.31	0.19	0.21	0.16
11.5	0.06	0.30	-	-	-	-	0.38	0.21	0.34	0.17	0.25	0.41	0.38	0.24	0.28	0.24
15	0.16	0.40	0.13	0.13	0.14	0.06	0.47	0.33	0.39	0.23	0.33	0.45	0.45	0.31	0.36	0.34
20	0.39	0.49	0.18	0.17	0.19	0.08	0.55	0.42	0.42	0.26	0.39	0.50	0.51	0.36	0.41	0.40
21	0.43	0.52	0.19	0.18	0.20	0.09	0.57	0.42	0.42	0.27	0.40	0.52	0.53	0.37	0.41	0.41
25	0.49	0.56	0.22	0.18	0.22	0.13	0.60	0.43	0.44	0.31	0.43	0.53	0.54	0.41	0.45	0.41
30	0.54	0.61	0.24	0.19	0.25	0.27	0.63	0.49	0.47	0.39	0.50	0.55	0.55	0.51	0.53	0.44
35	0.56	0.65	0.26	0.20	0.28	0.46	0.64	0.58	0.53	0.63	0.60	0.57	0.58	0.64	0.63	0.48
38	0.57	0.66	0.27	0.20	0.30	0.61	0.64	0.64	0.58	0.82	0.67	0.58	0.59	0.74	0.70	0.53

Femur length and biparietal diameter measurements adopted for phantom construction from Guihard-Costa et al. Dashes indicate the corresponding phantom was not constructed.

Table 2.

Gestational Age (weeks PC)	Femur Length (mm)			Biparietal Diameter (mm)		
	10 th PCTL	50 th PCTL	90 th PCTL	10 th PCTL	50 th PCTL	90 th PCTL
10	-	10	-	-	21	-
15	-	25	-	-	39	-
20	37	39	42	51	54	58
25	49	52	55	67	70	73
30	60	63	66	78	82	86
35	69	72	76	86	90	95
38	72	77	81	88	95	99

Table 3.

Densities (g cm^{-3}), masses (g) and % difference from target values for tissues in 50th percentile UF fetal hybrid phantoms.^a

Organ System	UFH08WK50			UFH10WK50			UFH15WK50			UFH20WK50			UFH25WK50			UFH30WK50			UFH35WK50			UFH38WK50		
	Phantom		Density	Phantom		Density	Phantom		Density	Phantom		Density	Phantom		Density	Phantom		Density	Phantom		Density	Phantom		Density
	Mass	%Diff.		Mass	%Diff.		Mass	%Diff.		Mass	%Diff.		Mass	%Diff.		Mass	%Diff.		Mass	%Diff.		Mass	%Diff.	
Respiratory System																								
ET1 (anterior nasal layer)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
ET2 (posterior nasal layer)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
ET2 (oral cavity layer)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
ET2 (larynx)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
ET2 (pharynx)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Trachea - wall	1.07	9.89E-04	-	1.07	6.59E-03	-	1.07	3.71E-02	-	1.07	1.22E-01	-	1.07	2.36E-01	-	1.07	3.44E-01	-	1.07	3.96E-01	-	1.07	4.99E-01	-
Bronchi - extrapulmonary	1.07	3.77E-04	-	1.07	2.49E-03	-	1.07	1.22E-02	-	1.07	4.62E-02	-	1.07	8.94E-02	-	1.07	1.30E-01	-	1.07	3.64E-01	-	1.07	4.59E-01	-
Lungs (2)	1.04	6.46E-02	0.45	1.04	4.97E-01	-0.55	1.04	4.67E+00	-0.64	1.04	1.19E+01	-0.69	1.04	2.05E+01	-0.58	1.04	3.10E+01	-0.58	0.62	4.70E+01	0.00	0.62	5.05E+01	-0.54
Alimentary System																								
Tongue	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Salivary glands ^b	1.03	3.09E-03	-	1.03	1.41E-02	-	1.03	9.01E-02	-	1.03	5.06E-01	-	1.03	9.67E-01	-	1.03	1.57E+00	-	1.03	5.10E+00	-	1.03	6.00E+00	-
Tonsils	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Esophagus - wall	1.03	2.62E-03	-	1.03	1.66E-02	-	1.03	9.06E-02	-	1.03	2.98E-01	-	1.03	5.78E-01	-	1.03	8.40E-01	-	1.03	1.55E+00	-	1.03	1.98E+00	-
Stomach - wall	1.03	5.74E-03	-	1.03	3.79E-02	-	1.03	8.86E-02	-	1.03	2.91E-01	-	1.03	5.65E-01	-	1.03	8.21E-01	-	1.03	5.55E+00	-	1.03	7.00E+00	-
Stomach - contents	1.00	7.63E-03	-	1.00	5.05E-02	-	1.00	1.10E-01	-	1.00	3.61E-01	-	1.00	6.99E-01	-	1.00	1.02E+00	-	1.00	1.95E+01	-	1.00	2.47E+01	-
Small Intestine	1.03	1.86E-02	-	1.03	3.54E-01	-	1.03	1.02E+00	-	1.03	3.21E+00	-	1.03	6.55E+00	-	1.03	1.11E+01	-	1.03	2.32E+01	-	1.03	2.92E+01	-
Wall	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Contents	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Colon - wall	1.03	3.59E-03	-	1.03	2.83E-02	-	1.03	1.30E-01	-	1.03	4.27E-01	-	1.03	8.27E-01	-	1.03	1.20E+00	-	1.03	5.16E+00	-	1.03	6.51E+00	-
Right	-	NI	-	-	-	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	-	-	-	-	
Left	-	NI	-	-	-	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	5.28E+00	-	1.03	6.66E+00	-
Rectosigmoid	-	NI	-	-	-	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	2.84E+00	-	1.03	3.59E+00	-
Colon - contents	1.00	2.77E-03	-	1.00	2.18E-02	-	1.00	1.00E-01	-	1.00	3.29E-01	-	1.00	6.38E-01	-	1.00	9.28E-01	-	1.00	1.12E+01	-	1.00	1.42E+01	-
Right	-	NI	-	-	-	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	-	-	-	-	-
Left	-	NI	-	-	-	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	1.40E+01	-	1.00	1.76E+01	-

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Organ System	UFH08WK50			UFH10WK50			UFH15WK50			UFH20WK50			UFH25WK50			UFH30WK50			UFH35WK50			UFH38WK50						
	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.				
	Density	Mass		Density	Mass		Density	Mass		Density	Mass		Density	Mass		Density	Mass		Density	Mass		Density	Mass		Density	Mass	Density	Mass
Rectosigmoid	-	NI	-	-	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	1.00	8.71E+00	-	1.00	1.10E+01	-	-
Liver	1.04	3.97E-01	-0.83	1.04	1.01E+00	0.00	1.04	7.14E+00	0.00	1.04	2.26E+01	-0.53	1.04	3.78E+01	0.06	1.04	6.12E+01	-0.01	1.04	1.04E+02	0.00	1.04	1.30E+02	0.00	1.04	1.30E+02	0.00	0.00
Gall Bladder	1.03	1.32E-03	-	1.03	8.71E-03	-	1.03	5.75E-02	-	1.03	1.89E-01	-	1.03	3.66E-01	-	1.03	5.32E-01	-	1.03	3.96E-01	-	1.03	4.99E-01	-	1.03	4.99E-01	-	-
Wall	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Contents	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.03	2.22E+00	-	1.03	2.80E+00	-	-
Pancreas	1.03	4.07E-04	0.00	1.03	2.78E-02	0.05	1.03	1.96E-01	0.00	1.03	6.00E-01	-0.08	1.03	1.01E+00	0.01	1.03	1.77E+00	-0.27	1.03	2.84E+00	0.00	1.03	3.65E+00	0.00	1.03	3.65E+00	0.02	0.02
Circulatory System																												
Heart (wall & contents)	1.04	6.86E-02	0.53	1.04	1.49E-01	-0.81	1.04	1.10E+00	0.04	1.04	3.38E+00	0.00	1.04	6.28E+00	-0.02	1.04	1.08E+01	-0.01	1.04	1.76E+01	0.00	1.04	2.03E+01	0.00	1.04	2.03E+01	0.00	0.00
	UFH08WK50			UFH10WK50			UFH15WK50			UFH20WK50			UFH25WK50			UFH30WK50			UFH35WK50			UFH38WK50						
	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	
Density	Mass	Density		Mass	Density		Mass	Density		Mass	Density		Mass	Density		Mass	Density		Mass	Density		Mass	Density		Mass	Density		Mass
Kidneys (all regions)	1.03	1.36E-02	-0.70	1.03	1.60E-01	-0.06	1.03	1.30E+00	-0.02	1.03	4.24E+00	0.17	1.03	8.53E+00	0.00	1.03	1.50E+01	-0.20	1.03	2.25E+01	0.00	1.03	2.57E+01	0.00	1.03	2.57E+01	0.00	0.00
Urinary Bladder - wall	1.04	9.69E-04	-	1.04	6.41E-03	-	1.04	5.15E-02	-	1.04	1.70E-01	-	1.04	3.29E-01	-	1.04	4.78E-01	-	1.04	3.17E+00	-	1.04	4.00E+00	-	1.04	4.00E+00	-	-
Urinary Bladder - contents	1.01	5.24E-04	-	1.01	3.46E-03	-	1.01	6.22E-02	-	1.01	2.05E-01	-	1.01	3.96E-01	-	1.01	5.76E-01	-	1.01	7.56E+00	-	1.01	9.55E+00	-	1.01	9.55E+00	-	-
Penis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5.97E-01	-	1.05	7.54E-01	-	1.05	7.54E-01	-	-
Scrotum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.27E+00	-	1.03	1.60E+00	-	1.03	1.60E+00	-	-
Testes (2)	1.04	1.43E-03	-	1.04	9.48E-03	-	1.04	1.17E-02	-	1.04	3.86E-02	-	1.04	7.49E-02	-	1.04	1.09E-01	-	1.04	6.73E-01	-	1.04	8.50E-01	-	1.04	8.50E-01	-	-
Prostate Gland	-	-	-	-	-	-	-	-	-	1.03	3.00E-03	-	1.03	5.82E-03	-	1.03	8.46E-03	-	1.03	6.34E-01	-	1.03	8.00E-01	-	1.03	8.00E-01	-	-
Ovaries (2)	1.05	1.32E-03	-	1.05	8.71E-03	-	1.05	4.04E-02	-	1.05	1.33E-01	-	1.05	1.68E-01	-	1.05	2.03E-01	-	1.05	2.38E-01	-	1.05	3.00E-01	-	1.05	3.00E-01	-	-
Uterus	1.03	1.06E-03	-	1.03	7.00E-03	-	1.03	4.17E-02	-	1.03	1.37E-01	-	1.03	2.66E-01	-	1.03	3.87E-01	-	1.05	3.17E+00	-	1.05	4.00E+00	-	1.05	4.00E+00	-	-
Skeletal System																												
Cartilage/Fibrous Tissue																												
Cranium	1.10	1.02E-01	-	1.10	4.38E-01	-	1.10	8.76E+00	-	1.10	1.66E+01	-	1.10	2.78E+01	-	1.10	4.02E+01	-	-	-	-	-	-	-	-	-	-	-
Cranial cartilage	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	1.34E+01	-	1.10	1.57E+01	-	1.10	1.57E+01	-	-
Bone-associated cartilage	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	NI	-	-	4.85E+01	-	1.10	5.49E+01	-	1.10	5.49E+01	-	-
Mandible & postcranial skeleton	1.10	NR	-	1.10	NR	-	1.10	NR	-	1.10	NR	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Costal cartilage	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	9.54E+00	-	1.10	1.20E+01	-	1.10	1.20E+01	-	-
Intervertebral discs	-	-	-	-	-	-	-	-	-	1.10	5.92E-01	-	1.10	1.15E+00	-	1.10	1.67E+00	-	-	9.82E-01	-	1.10	1.38E+00	-	1.10	1.38E+00	-	-

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Organ System	UFH08WK50			UFH10WK50			UFH15WK50			UFH20WK50			UFH25WK50			UFH30WK50			UFH35WK50			UFH38WK50		
	Phantom		Density	Phantom		Density	Phantom		Density	Phantom		Density	Phantom		Density	Phantom		Density	Phantom		Density	Phantom		Density
	Mass	%Diff.		Mass	%Diff.		Mass	%Diff.		Mass	%Diff.		Mass	%Diff.		Mass	%Diff.		Mass	%Diff.		Mass	%Diff.	
Bone-associated cartilage	1.10	-	1.10	1.62E+00	-	1.10	6.76E+00	-	1.10	2.03E+01	-	1.10	3.72E+01	-	1.10	4.92E+01	-	1.10	6.72E+01	-	1.10	7.58E+01	-	-
Homogeneous Bone	-	-	1.12	2.69E-02	-	1.18	1.81E+00	-	1.24	1.20E+01	-													
Cranium												1.30	3.16E+01	-	1.36	5.82E+01	-	1.42	1.02E+02	-	1.46	1.26E+02	-	-
Mandible	-	-	1.12	1.41E-02	-	1.16	2.73E-01	-	1.21	9.96E-01	-	1.25	2.26E+00	-	1.3	4.13E+00	-	1.34	7.63E+00	-	1.37	9.37E+00	-	-
Postcranial skeleton	-	-	1.12	2.97E-01	-	1.16	2.64E+00	-	1.21	1.04E+01	-	1.25	2.35E+01	-	1.3	4.23E+01	-	1.34	1.19E+02	-	1.37	1.66E+02	-	-
Additional Tissues																								
Adrenal Glands (2)	1.03	1.98E-02	-0.84	1.03	1.00E-01	0.22	1.03	6.40E-01	-0.06	1.03	1.73E+00	-0.06	1.03	2.58E+00	0.01	1.03	4.07E+00	0.05	1.03	6.46E+00	0.01	1.03	7.76E+00	0.10
Brain	1.02	7.00E-01	0.00	1.02	3.20E+00	-0.02	1.02	2.28E+01	0.14	1.02	6.38E+01	0.15	1.02	1.18E+02	0.10	1.02	2.06E+02	0.18	1.03	3.19E+02	0.00	1.03	3.68E+02	0.01
Breasts (2)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.99	7.14E-02	-	0.99	9.01E-02	-
Eyeballs (2)	1.03	1.57E-02	-	1.03	7.16E-02	-	1.03	3.44E-01	-	1.03	9.81E-01	-	1.03	1.88E+00	-	1.03	3.04E+00	-	1.03	5.00E+00	-	1.03	5.88E+00	-
Lens (2)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.07	1.10E-01	-	1.07	1.29E-01	-
Pituitary Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.03	8.50E-02	-	1.03	9.99E-02	-
Residual Soft Tissue	1.03	1.86E+00	-	1.03	1.28E+01	-	1.03	8.43E+01	-	1.03	2.83E+02	-	1.03	6.44E+02	-	1.03	1.12E+03	-	1.03	1.57E+03	-	1.03	2.01E+03	-
Spinal Cord	1.02	3.33E-03	-	1.02	2.20E-02	-	1.02	1.88E-01	-	1.02	6.17E-01	-	1.02	1.24E+00	-	1.02	1.74E+00	-	1.03	4.41E+00	-	1.03	6.58E+00	-
Spleen	1.04	8.54E-04	-0.03	1.04	1.00E-02	-0.01	1.04	1.50E-01	-0.14	1.04	6.60E-01	0.06	1.04	1.78E+00	-0.23	1.04	4.38E+00	0.18	1.04	8.11E+00	-0.01	1.04	1.02E+01	0.03
Thymus	1.07	5.43E-04	0.32	1.07	1.00E-02	0.00	1.07	2.00E-01	0.04	1.07	9.20E-01	0.01	1.07	2.37E+00	0.01	1.07	4.91E+00	-0.02	1.07	8.95E+00	-0.01	1.07	1.02E+01	-0.04
Thyroid	1.05	3.33E-03	-	1.05	2.20E-02	-	1.05	7.66E-02	-	1.05	1.80E-01	-	1.05	3.60E-01	-	1.05	6.34E-01	-	1.05	1.00E+00	-0.04	1.05	1.30E+00	-0.01
Trachea & bronchi - contents	1.00	8.76E-04	-	1.00	5.77E-03	-	1.00	2.64E-02	-	1.00	9.01E-02	-	1.00	1.75E-01	-	1.00	2.54E-01	-	1.00	9.17E-01	-	1.00	1.04E+00	-
Total Mass	1.04	3.58	0.33	1.04	21.18	0.85	1.04	146.34	0.93	1.04	467.14	-0.61	1.05	988.28	-0.17	1.05	1692.51	-0.44	1.04	2642.66	0.67	1.05	3299.39	0.74

Dash - Not defined in phantom and/or not applicable

NI - Present in phantom but not as an independent structure/volume

NR - Present in phantom as an independent structure/volume but not reported

^aSee Table 6 for density and target masses specifics

^bSalivary glands include parotid, submaxillary and sublingual glands

Table 4.

Densities (g cm^{-3}), masses (g) and % difference from target values for tissues in 10th percentile UF fetal hybrid phantoms. ^a

Organ System	UFH20WK10			UFH25WK10			UFH30WK10			UFH35WK10			UFH38WK10		
	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.
Respiratory System															
ET1 (anterior nasal layer)	-	-	-	-	-	-	-	-	-	1.03	9.77E-02	-	1.03	1.04E-01	-
ET2 (posterior nasal layer)	-	-	-	-	-	-	-	-	-	1.03	8.94E-01	-	1.03	9.50E-01	-
ET2 (oral cavity layer)	-	-	-	-	-	-	-	-	-	1.03	5.49E-01	-	1.03	5.83E-01	-
ET2 (larynx)	-	-	-	-	-	-	-	-	-	1.07	9.07E-01	-	1.07	1.06E+00	-
ET2 (pharynx)	-	-	-	-	-	-	-	-	-	1.03	2.15E-01	-	1.03	2.10E-01	-
Trachea - wall	1.07	9.60E-02	-	1.07	1.98E-01	-	1.07	2.97E-01	-	1.07	3.48E-01	-	1.07	4.08E-01	-
Bronchi - extrapulmonary	1.07	3.63E-02	-	1.07	7.48E-02	-	1.07	1.12E-01	-	1.07	3.20E-01	-	1.07	3.76E-01	-
Lungs (2)	1.04	7.12E+00	-0.24	1.04	1.18E+01	-0.62	1.04	1.96E+01	-0.34	0.62	3.01E+01	0.00	0.62	3.10E+01	0.00
Alimentary System															
Tongue	-	-	-	-	-	-	-	-	-	1.05	2.62E+00	-	1.05	2.78E+00	-
Salivary glands ^b	1.03	4.26E-01	-	1.03	8.48E-01	-	1.03	1.34E+00	-	1.03	4.49E+00	-	1.03	4.77E+00	-
Tonsils	-	-	-	-	-	-	-	-	-	1.03	7.48E-02	-	1.03	7.94E-02	-
Esophagus - wall	1.03	2.34E-01	-	1.03	4.83E-01	-	1.03	7.25E-01	-	1.03	1.38E+00	-	1.03	1.52E+00	-
Stomach - wall	1.03	2.29E-01	-	1.03	4.72E-01	-	1.03	7.09E-01	-	1.03	4.88E+00	-	1.03	5.72E+00	-
Stomach - contents	1.00	2.84E-01	-	1	5.85E-01	-	1	8.77E-01	-	1	1.72E+01	-	1	2.02E+01	-
Small Intestine	1.03	2.59E+00	-	1.03	5.32E+00	-	1.03	6.88E+00	-	1.03	2.04E+01	-	1.03	2.39E+01	-
Wall	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contents	-	-	-	-	-	-	-	-	-	1	2.11E+01	-	1	2.47E+01	-
Colon - wall	1.03	3.36E-01	-	1.03	6.92E-01	-	1.03	1.04E+00	-	1.03	4.54E+00	-	1.03	5.32E+00	-
Right	-	NI	-	-	NI	-	-	NI	-	-	-	-	-	-	-
Left	-	NI	-	-	NI	-	-	NI	-	1.03	4.64E+00	-	1.03	5.44E+00	-
Rectosigmoid	-	NI	-	-	NI	-	-	NI	-	1.03	2.50E+00	-	1.03	2.93E+00	-
Colon - contents	1.00	2.59E-01	-	1	5.34E-01	-	1	8.01E-01	-	1	9.88E+00	-	1	1.16E+01	-

Organ System	UFH20WK10			UFH25WK10			UFH30WK10			UFH35WK10			UFH38WK10		
	Density	Phantom	%Diff.	Density	Phantom	Mass	%Diff.	Density	Phantom	Mass	%Diff.	Density	Phantom	Mass	%Diff.
Right	-	NI	-	-	NI	NI	-	-	-	NI	-	-	-	-	-
Left	-	NI	-	-	NI	NI	-	-	-	1.23E+01	-	1	1.44E+01	-	-
Rectosigmoid	-	NI	-	-	NI	NI	-	-	-	7.66E+00	-	1	8.98E+00	-	-
Liver	1.04	1.54E+01	0.00	1.04	2.50E+01	-0.39	-	1.04	3.94E+01	0.00	0.00	1.04	8.90E+01	-0.02	-
Gall Bladder	1.03	1.49E-01	-	1.03	3.06E-01	-	-	1.03	4.60E-01	-	-	1.03	4.08E-01	-	-
Wall	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contents	-	-	-	-	-	-	-	-	-	1.95E+00	-	1.03	2.29E+00	-	-
Pancreas	1.03	2.67E-01	-0.04	1.03	5.24E-01	-0.01	-	1.03	1.17E+00	0.01	0.00	1.03	2.18E+00	0.03	0.03
Circulatory System															
Heart (wall & contents)	1.04	2.33E+00	0.02	1.04	3.92E+00	0.00	0.00	1.04	6.96E+00	0.00	0.00	1.04	1.39E+01	0.00	0.00
Urogenital System															
Kidneys (all regions)	1.03	2.72E+00	0.00	1.03	5.29E+00	-0.01	-	1.03	9.37E+00	-0.01	-	1.03	1.61E+01	0.00	0.00
Urinary Bladder - wall	1.04	1.33E-01	-	1.04	2.75E-01	-	-	1.04	4.13E-01	-	-	1.04	3.27E+00	-	-
Urinary Bladder - contents	1.01	1.61E-01	-	1.01	3.32E-01	-	-	1.01	4.98E-01	-	-	1.01	7.80E+00	-	-
Penis	-	-	-	-	-	-	-	-	-	5.26E-01	-	1.05	6.16E-01	-	-
Scrotum	-	-	-	-	-	-	-	-	-	1.12E+00	-	1.03	1.31E+00	-	-
Testes (2)	1.04	3.04E-02	-	1.04	6.26E-02	-	-	1.04	9.40E-02	-	-	1.04	6.95E-01	-	-
Prostate Gland	1.03	2.36E-03	-	1.03	4.87E-03	-	-	1.03	7.30E-03	-	-	1.03	6.54E-01	-	-
Ovaries (2)	1.05	1.04E-01	-	1.05	1.39E-01	-	-	1.05	1.74E-01	-	-	1.05	2.46E-01	-	-
Uterus	1.03	1.08E-01	-	1.03	2.22E-01	-	-	1.03	3.34E-01	-	-	1.05	3.27E+00	-	-
Skeletal System															
Cartilage/Fibrous Tissue	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cranium	1.10	1.40E+01	-	1.10	2.44E+01	-	-	1.10	3.43E+01	-	-	-	-	-	-
Cranial cartilage	-	NI	-	-	NI	-	-	-	NI	-	-	1.10	1.18E+01	1.10	1.25E+01
Bone-associated cartilage	-	NI	-	-	NI	-	-	-	NI	-	-	1.10	4.27E+01	1.10	4.36E+01
Mandible & postcranial skeleton	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Organ System	UFH20WK10			UFH25WK10			UFH30WK10			UFH35WK10			UFH38WK10		
	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.
Costal cartilage	1.10	NR	-	1.10	NR	-	1.10	NR	-	1.10	8.40E+00	-	1.10	9.84E+00	-
Intervertebral discs	1.10	4.65E-01	-	1.10	9.60E-01	-	1.10	1.44E+00	-	1.10	9.56E-01	-	1.10	1.13E+00	-
Bone-associated cartilage	1.10	1.67E+01	-	1.10	3.05E+01	-	1.10	4.15E+01	-	1.10	5.92E+01	-	1.10	6.19E+01	-
<i>Homogeneous Bone</i>	1.24	1.01E+01	-	1.30	2.77E+01	-	1.36	4.96E+01	-	1.42	8.95E+01	-	1.46	1.00E+02	-
Cranium															
Mandible	1.21	8.39E-01	-	1.25	1.98E+00	-	1.30	3.52E+00	-	1.34	6.72E+00	-	1.37	7.45E+00	-
Postcranial skeleton	1.21	8.18E+00	-	1.25	1.93E+01	-	1.30	3.57E+01	-	1.34	1.09E+02	-	1.37	1.35E+02	-
Additional Tissues															
Adrenal Glands (2)	1.03	1.00E+00	-0.03	1.03	1.31E+00	0.01	1.03	2.15E+00	-0.03	1.03	3.77E+00	0.00	1.03	4.14E+00	0.00
Brain	1.02	4.83E+01	0.00	1.02	9.11E+01	0.02	1.02	1.61E+02	0.05	1.03	2.63E+02	0.00	1.03	3.03E+02	0.00
Breasts (2)	-	-	-	-	-	-	-	-	-	0.99	3.62E-01	-	0.99	4.25E-01	-
Eyeballs (2)	1.03	8.27E-01	-	1.03	1.64E+00	-	1.03	2.59E+00	-	1.03	4.39E+00	-	1.03	4.67E+00	-
Lens (2)	-	-	-	-	-	-	-	-	-	1.07	1.03E-01	-	1.07	1.03E-01	-
Pituitary Gland	-	-	-	-	-	-	-	-	-	1.03	7.92E-02	-	1.03	7.94E-02	-
Residual Soft Tissue	1.03	2.42E+02	-	1.03	5.15E+02	-	1.03	9.61E+02	-	1.03	1.39E+03	-	1.03	1.86E+03	-
Spinal Cord	1.02	4.85E-01	-	1.02	1.04E+00	-	1.02	1.50E+00	-	1.03	4.13E+00	-	1.03	5.50E+00	-
Spleen	1.04	3.02E-01	0.00	1.04	8.71E-01	0.03	1.04	1.97E+00	-0.08	1.04	3.89E+00	0.02	1.04	5.21E+00	0.01
Thymus	1.07	4.46E-01	-0.05	1.07	1.06E+00	0.05	1.07	1.80E+00	0.00	1.07	4.59E+00	0.00	1.07	5.21E+00	0.00
Thyroid	1.05	1.41E-01	-	1.05	3.01E-01	-	1.05	5.48E-01	-	1.05	7.27E-01	-	1.05	1.06E+00	-
Trachea & bronchi - contents	1.00	7.09E-02	-	1.00	1.04E-01	-	1.00	2.19E-01	-	1.00	9.17E-01	-	1.00	8.29E-01	-
Total	1.04	378.54	0.94	1.05	777.98	-0.26	1.05	1397.49	-0.18	1.05	2267.12	0.76	1.05	2865.77	0.55

Dash - Not defined in phantom and/or not applicable

NI - Present in phantom but not as an independent structure/volume

NR - Present in phantom as an independent structure/volume but not reported

Salivary glands include parotid, submaxillary and sublingual glands
 q
See Table 6 for density and target masses specifics
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Table 5.

Densities (g cm^{-3}), masses (g) and % difference from target values for tissues in 90th percentile UF fetal hybrid phantoms. ^a

Organ System	UFH20WK90			UFH25WK90			UFH30WK90			UFH35WK90			UFH38WK90		
	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.
Respiratory System															
ET1 (anterior nasal layer)	-	-	-	-	-	-	-	-	-	1.03	1.30E-01	-	1.03	1.48E-01	-
ET2 (posterior nasal layer)	-	-	-	-	-	-	-	-	-	1.03	1.19E+00	-	1.03	1.35E+00	-
ET2 (oral cavity layer)	-	-	-	-	-	-	-	-	-	1.03	7.34E-01	-	1.03	8.31E-01	-
ET2 (larynx)	-	-	-	-	-	-	-	-	-	1.07	1.21E+00	-	1.07	1.51E+00	-
ET2 (pharynx)	-	-	-	-	-	-	-	-	-	1.03	3.06E-01	-	1.03	4.28E-01	-
Trachea - wall	1.07	1.52E-01	-	1.07	2.80E-01	-	1.07	3.95E-01	-	1.07	4.66E-01	-	1.07	5.81E-01	-
Bronchi - extrapulmonary	1.07	5.76E-02	-	1.07	1.06E-01	-	1.07	1.49E-01	-	1.07	4.28E-01	-	1.07	5.35E-01	-
Lungs (2)	1.04	1.68E+01	-0.60	1.04	2.91E+01	-0.54	1.04	4.25E+01	-0.46	0.62	6.39E+01	0.00	0.62	7.06E+01	0.00
Alimentary System															
Tongue	-	-	-	-	-	-	-	-	-	1.05	3.50E+00	-	1.05	3.96E+00	-
Salivary glands ^b	1.03	6.32E-01	-	1.03	1.10E+00	-	1.03	1.82E+00	-	1.03	6.00E+00	-	1.03	6.79E+00	-
Tonsils	-	-	-	-	-	-	-	-	-	1.03	9.99E-02	-	1.03	1.13E-01	-
Esophagus - wall	1.03	3.72E-01	-	1.03	6.84E-01	-	1.03	9.65E-01	-	1.03	1.87E+00	-	1.03	2.18E+00	-
Stomach - wall	1.03	3.64E-01	-	1.03	6.68E-01	-	1.03	9.44E-01	-	1.03	6.52E+00	-	1.03	8.15E+00	-
Stomach - contents	1.00	4.50E-01	-	1.00	8.27E-01	-	1	1.17E+00	-	1.00	2.30E+01	-	1.00	2.87E+01	-
Small Intestine	1.03	4.19E+00	-	1.03	7.56E+00	-	1.03	1.30E+01	-	1.03	2.72E+01	-	1.03	3.40E+01	-
Wall	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contents	-	-	-	-	-	-	-	-	-	1.00	2.82E+01	-	1.00	3.52E+01	-
Colon - wall	1.03	5.33E-01	-	1.03	9.78E-01	-	1.03	1.38E+00	-	1.03	6.07E+00	-	1.03	7.58E+00	-
Right	-	NI	-	-	NI	-	-	NI	-	-	-	-	-	-	-
Left	-	NI	-	-	NI	-	-	NI	-	1.03	6.20E+00	-	1.03	7.75E+00	-
Rectosigmoid	-	NI	-	-	NI	-	-	NI	-	1.03	3.34E+00	-	1.03	4.17E+00	-

Organ System	UFH20WK90			UFH25WK90			UFH30WK90			UFH35WK90			UFH38WK90		
	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.	Density	Phantom	%Diff.
Colon - contents	1.00	4.11E-01	-	1.00	7.55E-01	-	1.00	1.07E+00	-	1.00	1.32E+01	-	1.00	1.65E+01	-
Right	-	NI	-	-	NI	-	-	-	-	-	-	-	-	-	-
Left	-	NI	-	-	NI	-	-	-	-	1.00	1.64E+01	-	1.00	2.05E+01	-
Rectosigmoid	-	NI	-	-	NI	-	-	-	-	1.00	1.02E+01	-	1.00	1.28E+01	-
Liver	1.04	2.98E+01	-0.76	1.04	5.02E+01	-0.63	1.04	8.23E+01	-0.83	1.04	1.33E+02	-0.15	1.04	1.70E+02	-0.55
Gall Bladder	1.03	2.36E-01	-	1.03	4.33E-01	-	1.03	6.12E-01	-	1.03	4.65E-01	-	1.03	5.81E-01	-
Wall	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contents	-	-	-	-	-	-	-	-	-	1.03	2.61E+00	-	1.03	3.26E+00	-
Pancreas	1.03	9.32E-01	-0.08	1.03	1.50E+00	-0.05	1.03	2.37E+00	-0.03	1.03	3.93E+00	0.01	1.03	5.12E+00	0.01
Circulatory System															
Heart (wall & contents)	1.04	4.42E+00	-0.22	1.04	8.64E+00	0.01	1.04	1.46E+01	-0.54	1.04	2.30E+01	-0.52	1.04	2.67E+01	-0.01
Urogenital System															
Kidneys (all regions)	1.03	5.70E+00	-0.72	1.03	1.17E+01	-0.23	1.03	2.06E+01	-0.08	1.03	3.07E+01	0.00	1.03	3.53E+01	0.00
Urinary Bladder - wall	1.04	2.12E-01	-	1.04	3.89E-01	-	1.04	5.49E-01	-	1.04	3.73E+00	-	1.04	4.66E+00	-
Urinary Bladder - contents	1.01	2.55E-01	-	1.01	4.69E-01	-	1.01	6.62E-01	-	1.01	8.90E+00	-	1.01	1.11E+01	-
Penis	-	-	-	-	-	-	-	-	-	1.05	7.03E-01	-	1.05	8.78E-01	-
Scrotum	-	-	-	-	-	-	-	-	-	1.03	1.50E+00	-	1.03	1.87E+00	-
Testes (2)	1.04	4.82E-02	-	1.04	8.86E-02	-	1.04	1.25E-01	-	1.04	7.92E-01	-	1.04	9.89E-01	-
Prostate Gland	1.03	3.75E-03	-	1.03	6.88E-03	-	1.03	9.72E-03	-	1.03	7.46E-01	-	1.03	9.32E-01	-
Ovaries (2)	1.05	1.66E-01	-	1.05	2.04E-01	-	1.05	2.42E-01	-	1.05	2.80E-01	-	1.05	3.50E-01	-
Uterus	1.03	1.71E-01	-	1.03	3.15E-01	-	1.03	4.44E-01	-	1.05	3.73E+00	-	1.05	4.66E+00	-
Skeletal System															
Cartilage/Fibrous Tissue															
Cranium	1.10	2.07E+01	-	1.10	3.15E+01	-	1.10	4.67E+01	-	-	-	-	-	-	-
Cranial cartilage	-	NI	-	-	NI	-	-	NI	-	1.10	1.57E+01	-	1.10	1.78E+01	-

Organ System	UFH20WK90			UFH25WK90			UFH30WK90			UFH35WK90			UFH38WK90		
	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.	Phantom		%Diff.
	Density	Mass		Density	Mass		Density	Mass		Density	Mass		Density	Mass	
Bone-associated cartilage	-	NI	-	-	NI	-	-	NI	-	1.10	5.71E+01	-	1.10	6.21E+01	-
Mandible & postcranial skeleton															
Costal cartilage	1.10	NR	-	1.10	NR	-	1.10	NR	-	1.10	1.12E+01	-	1.10	1.40E+01	-
Intervertebral discs	1.10	7.39E-01	-	1.10	1.36E+00	-	1.10	1.92E+00	-	1.10	1.28E+00	-	1.10	1.60E+00	-
Bone-associated cartilage	1.10	2.56E+01	-	1.10	4.43E+01	-	1.10	5.73E+01	-	1.10	7.77E+01	-	1.10	8.81E+01	-
Homogeneous Bone															
Cranium	1.24	1.49E+01	-	1.30	3.59E+01	-	1.36	6.75E+01	-	1.42	1.20E+02	-	1.46	1.43E+02	-
Mandible	1.21	1.24E+00	-	1.25	2.56E+00	-	1.30	4.79E+00	-	1.34	8.98E+00	-	1.37	1.06E+01	-
Postcranial skeleton	1.21	1.30E+01	-	1.25	2.76E+01	-	1.30	5.02E+01	-	1.34	1.46E+02	-	1.37	1.93E+02	-
Additional Tissues															
Adrenal Glands (2)	1.03	2.47E+00	0.35	1.03	3.85E+00	0.13	1.03	5.99E+00	0.00	1.03	9.12E+00	-0.34	1.03	1.14E+01	0.39
Brain	1.02	7.91E+01	0.00	1.02	1.45E+02	0.00	1.02	2.51E+02	0.01	1.03	3.75E+02	-0.04	1.03	4.33E+02	0.00
Breasts (2)	-	-	-	-	-	-	-	-	-	0.99	4.84E-01	-	0.99	6.05E-01	-
Eyeballs (2)	1.03	1.23E+00	-	1.03	2.13E+00	-	1.03	3.53E+00	-	1.03	5.88E+00	-	1.03	6.65E+00	-
Lens (2)	-	-	-	-	-	-	-	-	-	1.07	1.29E-01	-	1.07	1.47E-01	-
Pituitary Gland	-	-	-	-	-	-	-	-	-	1.03	9.99E-02	-	1.03	1.13E-01	-
Residual Soft Tissue	1.03	3.48E+02	-	1.03	7.36E+02	-	1.03	1.29E+03	-	1.03	1.78E+03	-	1.03	2.27E+03	-
Spinal Cord	1.02	7.70E-01	-	1.02	1.47E+00	-	1.02	2.00E+00	-	1.03	5.99E+00	-	1.03	6.82E+00	-
Spleen	1.04	1.02E+00	-0.28	1.04	2.69E+00	0.00	1.04	6.76E+00	-0.10	1.04	1.23E+01	0.00	1.04	1.51E+01	-0.33
Thymus	1.07	1.38E+00	-0.65	1.07	3.68E+00	0.01	1.07	8.02E+00	0.01	1.07	1.32E+01	-0.69	1.07	1.52E+01	0.00
Thyroid	1.05	2.24E-01	-	1.05	4.26E-01	-	1.05	7.29E-01	-	1.05	1.18E+00	-	1.05	1.51E+00	-
Trachea & bronchi - contents	1.00	1.13E-01	-	1.00	2.07E-01	-	1.00	2.92E-01	-	1.00	9.38E-01	-	1.00	1.21E+00	-
Total	1.04	579.25	0.74	1.05	1161.11	0.10	1.05	1998.01	-0.10	1.04	3073.02	0.75	1.05	3823.31	0.61

(-) Not defined in phantom and/or not applicable

(NI) Present in phantom but not as an independent structure/volume

Salivary glands include parotid, submaxillary and sublingual glands

See Table 6 for density and target masses specifics

Present in phantom as an independent structure/volume but not reported

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Table 6.

Comments regarding sources of fetal organ masses, tissue compositions, and mass densities.

Organ System	Ages where present (weeks PC)	Density Comment	Target Mass Comments
Respiratory System			
ET1 (anterior nasal layer)	35,38	Average male soft tissue - adult	4,5 6,7
ET2 (posterior nasal layer)	35,38	Average male soft tissue - adult	4,5 6,7
ET2 (oral cavity layer)	35,38	Average male soft tissue - adult	4,5 6,7
ET2 (larynx)	35,38	50:50 soft tissue/cartilage	4,5 6,7
ET2 (pharynx)	35,38	Average male soft tissue - adult	4,5 6,7
Trachea - wall	8 – 38	50:50 soft tissue/cartilage	1,2 4,5 6,7
Bronchi - extrapulmonary	8 – 38	50:50 soft tissue/cartilage	1,2 4,5 6,7 8,9,10
Lungs (2)	8 – 38	Fetal lung density (8–30 weeks; all percentiles)	12 14
		Lee et al 2010 (35,38 weeks; all percentiles)	
Alimentary System			
Tongue	35,38	Muscle - newborn	4,5 6,7
Salivary glands	8 – 38	Average male soft tissue - adult	3 1,2 8,9,10,11 4,7 5,6
Tonsils	35,38	Average male soft tissue - adult	4,5 6,7
Esophagus - wall	8 – 38	Gastrointestine	1,2 11,8,9,10 4,5 6,7
Stomach - wall	8 – 38	Gastrointestine	1,2 11,8,9,10 4,5 6,7
Stomach - contents	8 – 38	STP water density	1,2 11,8,9,10 4,5 6,7
Small Intestine	8 – 30 (as HV)	Gastrointestine	1,2 8,9,10,12
Wall	35,38	Gastrointestine	4,5 6,7
Contents	35,38	STP water density	4,5 6,7
Colon - wall	8 – 30 (as HV)	Gastrointestine	1,2 8,9,10,11
Right	35,38	Gastrointestine	4,5 6,7
Left	35,38	Gastrointestine	4,5 6,7
Rectosigmoid	35,38	Gastrointestine	4,5 6,7
Colon - contents	8 – 30 (as HV)	STP water density	1,2 8,9,10,11
Right	35,38	STP water density	4,5 6,7
Left	35,38	STP water density	4,5 6,7
Rectosigmoid	35,38	STP water density	4,5 6,7
Liver	8 – 38	Fetal liver	
Gall Bladder	8 – 30 (as HV)	Average male soft tissue - adult	1,2 8,9,10,12
Wall	35,38	Average male soft tissue - adult	4,5 6,7
Contents	35,38	Average male soft tissue - adult	4,5 6,7
Pancreas	8 – 38	Average male soft tissue - adult	12 16 14 (except 10,15 weeks)
Circulatory System			

Organ System	Ages where present (weeks PC)	Density Comment	Target Mass Comments
Heart (wall & contents)	8 – 30 (as HV)	Fetal heart	12 14
<i>Urogenital System</i>			
Kidneys (all regions)	8 – 38	Fetal kidney	12 14
Urinary Bladder - wall	8 – 38	Bladder - adult,empty	1,2 11,8,9,10 4,5 6,7
Urinary Bladder - contents	8 – 38	Urine of average density	1,2 11,8,9,10 4,5 6,7
Penis	35, 38	Muscle - newborn	4,5 6,7
Scrotum	35, 38	Muscle - newborn	4,5 6,7
Testes (2)	8 – 38	Testes - adult	1,2 11,8,9,10 4,5 6,7
Prostate Gland	20 – 38	Average male soft tissue - adult	1,2 11,8,9,10 4,5 6,7
Ovaries (2)	8 – 38	Adult ovary	1,2 11,8,9,10 4,5 6,7
Uterus	8 – 30	Muscle - newborn	1,2 11,8,9,10 4,5 6,7
	35, 38	Adult ovary	
<i>Skeletal System</i>			
<i>Cartilage/Fibrous Tissue</i>			
Cranium	8 – 30 (as HV)	Adult skeletal cartilage	Derived, age-dependent
Cranial cartilage	35,38	Adult skeletal cartilage	Derived, age-dependent
Bone-associated cartilage	35,38	Adult skeletal cartilage	Derived, age-dependent
Mandible & postcranial skeleton			
Costal cartilage	8 – 38	Adult skeletal cartilage	Derived, age-dependent
Intervertebral discs	15 – 38	Adult skeletal cartilage	2 8,9,10 4,5 6,7
Bone-associated cartilage	8 – 38	Adult skeletal cartilage	Derived, age-dependent
<i>Homogeneous Bone</i>			
Cranium	10 – 38	Derived, varies	Derived, age-dependent
Mandible	10 – 38	Derived, varies	Derived, age-dependent
Postcranial skeleton	10 – 38	Derived, varies	Derived, age-dependent
<i>Additional Tissues</i>			
Adrenal Glands (2)	8 – 38	Average male soft tissue - adult	12 14
Brain	8 – 38	Fetal brain	12 14
Breasts (2)	35, 38	Adipose - newborn #2	4,5 6,7
Eyeballs (2)	8 – 38	Average male soft tissue - adult	1,2 11,8,9,10 4,5 6,7
Lens (2)	35, 38	Lens - adult	4,5 6,7
Pituitary Gland	35, 38	Average male soft tissue - adult	4,5 6,7
Residual Soft Tissue	8 – 38	Average male soft tissue - adult	percentile-dependent
Spinal Cord	8 – 38	Fetal brain	4,5 6,7 2,8,9,10,11
Spleen	8 – 38	Fetal spleen	12 14
Thymus	8 – 38	ICRP 89 - Para 606	12 14

Organ System	Ages where present (weeks PC)	Density Comment	Target Mass Comments
Thyroid	8 – 38	Adult thyroid	13 6,7,8,9,10,11
Trachea & bronchi - contents	8 – 38	STP water density	
Total Mass	8 – 38	-	12 15

¹Volume scaled from 11.5 week specimen-specific phantom to UFH10WK50

²Volume scaled from 21 week specimen-specific phantom to UFH15WK50, UFH20WK50, UFH25WK50 and UFH30WK50

³Volume scaled from UFH newborn to 11.5 and 21 week specimen-specific phantoms

⁴Volume scaled from UFH newborn to UFH35WK50

⁵Volume scaled from UFH newborn to UFH38WK50

⁶Volume scaled from UFH38WK50 to UFH38WK10 and UFH38WK90

⁷Volume scaled from UFH35WK50 to UFH35WK10 and UFH35WK90

⁸Volume scaled from UFH30WK50 to UFH30WK10 and UFH30WK90

⁹Volume scaled from UFH25WK50 to UFH25WK10 and UFH25WK90

¹⁰Volume scaled from UFH20WK50 to UFH20WK10 and UFH20WK90

¹¹Volume scaled from UFH10WK50 to UFH08WK50

¹²Segmented from 8 week NMR images

¹³ICRP 89 (10 – 38 weeks; 50th percentile)

¹⁴Archie et al 2006 (10 – 38 weeks; all percentiles)

¹⁵Guihard-Costa 1995 (10 – 38 weeks; all percentiles)

¹⁶Derived (UFH10WK50 and UFH15WK50)