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REVIEW

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# Voxel-based computational models of real human anatomy: a review

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**Abstract** Computational models of human anatomy are mathematical representations of human anatomy designed to be used in dosimetry calculations. They have been used in dosimetry calculations for radiography, radiotherapy, nuclear medicine, radiation protection and to investigate the effects of low frequency electromagnetic fields. Tomographic medical imaging techniques have allowed the construction of digital three-dimensional computational models based on the actual anatomy of individual humans. These are called voxel models, tomographic models or phantoms. Their usefulness lies in their faithful representation of human anatomy and the flexibility they afford by being able to be scaled in size to match the required human dimensions. Segmenting medical images in order to make voxel models is very time-consuming so semi-automatic segmentation techniques are being developed. Some 21 whole or partial body models currently exist and more are being prepared. These models are listed and discussed.

## Introduction

A computational model of human anatomy is a mathematical representation of the external envelope of the human body shape together with the boundaries of the internal organs and tissues. The volumes that the organs define are filled with a medium that has the chemical elements that compose the tissues in the correct proportion and the tissue density tabulated in sources such as ICRU reports 44 [1], 46 [2] and ICRP publication 89 [3]. Computational models have been used extensively with radiation transport codes to estimate organ doses resulting from diagnostic radiology examinations [4], for the planning of radiotherapy treatment and for the calculation of radiation protection quantities. Radiation transport codes simulate, using Monte Carlo methods, the interactions of photons and charged particles as they travel through a medium.

The first computational models were the "mathematical" models of adults and children from the Oak Ridge National Laboratory (ORNL) [5, 6, 7, 8]. They were mathematical in the sense that equations for planes, spheres, cylinders, cones, ellipsoids and elliptical cylinders (or parts and combinations thereof) were used to represent internal organs. These shapes were fitted into a simple "torso" shaped as an elliptical cylinder that also enclosed volumes designated as arm bones. The models included a head, neck and legs. These mathematical models are known as "MIRD" type models (after the Medical Internal Radiation Dose Committee) [9, 10] and have external dimensions and internal organ dimensions and masses close to those of the ICRP "Reference Man" [11, 12]. However simple geometrical volumes described by equations do not accurately conform to the shape of real organs and do not fit alongside each other in the way human organs do. Furthermore, the constraints imposed by fitting defined shapes within an elliptical cylinder mean that their positioning is not anatomically realistic. Consequently (and despite being called "anthropomorphic") the MIRD type models resemble real human anatomy only vaguely.

The rapid advancement and increased use of medical imaging technology, specifically computed tomography (CT) and magnetic resonance imaging (MRI), has provided high resolution cross-sectional digital images of internal anatomy. The pixel data from such images, when extended into the third dimension become cuboidal volume elements called voxels. The data may be used to create a three-dimensional digital representation of the shape, volume and composition of human organs. Each voxel is defined so that it contains a uniform medium and is assigned an index that identifies it as belonging to a particular organ or tissue. These computational models have also been called tomographic models [13], voxel

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models and voxel phantoms [14]. The terms voxel model and tomographic model are used interchangeably and sometimes used together. This review will follow the lead of ICRU report 48 [15] and not refer to computational models as phantoms. The term "phantom" can be used to refer unambiguously to a material object designed to be experimentally irradiated in order to make measurements of physical quantities using radiation detectors that have been placed on or within the object.

## Existing voxel models

The first voxel model, a representation of a head and trunk from CT scans of a female cadaver, was reported in 1984 and used for the calculation of effective dose from dental radiography [16]. Excluding this early model, at present there have been some 21 (or so) partial or whole body tomographic models reported in the literature (Table 1). The production of voxel models has increased dramatically in recent years with 13 models appearing in the literature in the 3 years from 2001 to 2003, and with more in preparation [17].

Voxel models have been used with Monte Carlo techniques to calculate absorbed doses to human organs and tissues irradiated with ionising radiation in radiography [18, 19, 20, 21], for radiation protection purposes [14, 22, 23, 24] and for dosimetry of procedures involving internal radioactive sources [25, 26, 27, 28, 29]. Whole-body voxel tomographic models have also been used with finite-difference time-domain calculations to determine the specific energy absorption rate (SAR) from exposure to non-ionising electromagnetic fields [30, 31, 32] and induced current densities from low-frequency magnetic fields [33]. In addition, radiotherapy treatment planning involves making a small voxel model, limited to the region of interest, from CT images of the relevant body section of each individual patient [34].

A reason behind the continuing development of voxel models is the hope that the greater realism with which human anatomy is represented in voxel computational models will allow for more accurate organ doses to be calculated than is possible using MIRD models. At the very least, accurately characterising human anatomy will decrease the uncertainties associated with dose calculations determined using the mathematical MIRD models.

## Obtaining anatomical images

The large number of contiguous images that are necessary to build a voxel model are not easy to obtain. This difficulty in part explains why so few voxel models exist (until recently). The data sets that have been used to construct voxel models have come from four sources and are existing images from an extensive clinical CT examination, whole body CT of cadavers, whole body MRI of volunteers and from "Visible Human" projects. These projects are designed to produce high resolution MR, CT and digital photographic images with small slice intervals, from donated cadavers.

**Table 1** Existing voxel tomographic computational models

| Model | Reference | Images | Race | Age and sex | Subject | Comment |
|---|---|---|---|---|---|---|
| Child | [18] | CT | Caucasian | 7-year-old female | Leukemia patient | Small for age (5 to 7-year-old) |
| Baby | [18] | CT | Caucasian | 8-week-old female | Cadaver | |
| VoxelMan[a] | [49, 50] | CT | Caucasian | Adult male | Diffuse melanoma | Head and torso |
| NORMAN | [14, 30] | MRI | Caucasian | Adult male | | Only 10 ribs |
| Golem | [26, 42] | CT | Caucasian | 38-year-old male | Leukemia patient | |
| ADELAIDE | [51] | CT | Caucasian | 14-year-old female | Patient | Torso |
| VIP-man | [35] | Colour photos | Caucasian | 38-year-old male | Cadaver (VHP[b]) | One testicle only |
| Otoko | [20] | CT | Japanese | Adult male | | |
| UF newborn | [38] | CT | Caucasian | 6-day-old female | Cadaver | |
| UF 2 month | [38] | CT | Caucasian | 6-month-old (=2) male | Cadaver | Small for age |
| Visible-human | [23] | CT | Caucasian | 38-year-old male | Cadaver (VHP) | |
| Frank | [23, 52] | CT | Caucasian | 48-year-old male | Patient | Head and torso |
| Donna | [17, 52] | CT | Caucasian | 40-year-old female | Patient | |
| Helga | [17, 23] | CT | Caucasian | 26-year-old female | Patient | Legs absent below mid-thigh |
| Irene | [17, 23] | CT | Caucasian | 32-year-old female | Patient | |
| MAX[c] | [24] | | Caucasian | Modified VoxelMan | | Reference man dimensions |
| Nagaoka man | [32] | MRI | Japanese | 22-year-old male | Volunteer | |
| Nagaoka woman | [32] | MRI | Japanese | 22-year-old female | Volunteer | |
| KR-man | [37] | MRI | Korean | 28-year-old male | | |
| Un-named | [53] | CT | | 9-month-old male | | Head and torso |
| Pregnant woman | [54] | CT | | 30 weeks pregnant | | Part torso |

[a] VoxelMan has no arms or legs but is available as MANTISSUE3–6 with VIP-man's arms (crossed in front of body) or with arms at side of body as VOXTISS8.
[b] *VHP* Visible Human Project.
[c] *MAX* is VOXTISS8 with smaller arms and legs and modified to conform to the dimensions and anatomical measurements of Reference Man.

An extensive CT scan of the body results in the subject receiving a considerable exposure to ionising radiation, hence it is not ethical to recruit healthy (asymptomatic) volunteers. However, leukemia patients may be required to undergo whole body radiation therapy to treat their leukemia. In this situation a whole body CT scan may be performed with appropriate permission and the data sets have been used to construct voxel models (for example the CHILD and Golem models). An emerging source of medical images for the production of voxel models is PET-CT. A whole body CT is undertaken as part of a positron emission tomography (PET) examination. Most often this examination is performed when looking for, staging of, or following up cancer (e.g. osteosarcoma). While no voxel models have yet been constructed using images from this source, the author has access to several whole body CT paediatric data sets for the purpose.

Usually existing medical images of patients examined for clinical reasons are used. Even in this case, privacy and medical confidentiality issues restrict access to medical images. When clinical images are available they may not include the entire body. For example, images of the head (e.g. ADELAIDE) or lower legs may not be included in the examination and arms may be held out of the image (e.g. ADELAIDE, Helga, VoxelMan). Head and arms from another individual may be added later. For example MAX is the VoxelMan body with arms and legs from the Visible Human Project male. Parts of the shoulders and hips may be outside the acquired field of view (e.g. ADELAIDE, Visible Human Project male CT images). In this case the images are manually edited to add any missing anatomy. When existing clinical images are used they may not be ideal for segmentation. Contrast medium may be present and obscure some detail and the pixel size and slice interval may be greater than desired.

The limitations on pixel resolution, field of view and slice separation imposed by clinical examinations of live patients and the possibility of movement are not present when cadavers are imaged. When cadavers are scanned, the concern about radiation exposure is absent so slice interval can be reduced. For the purpose of producing high resolution tomographic images of male and female anatomy, the US National Library of Medicine began the Visible Human Project (http://www.nlm.nih.gov/research/visible/visible_human.html). In 1994 MR, CT images and photographic images of the frozen and sequentially sectioned cadaver were made available. The latter process (producing photographic images) results in the destruction of the cadaver. Visible Human Project images have been segmented to produce the voxel models known as VIP-Man [35] and Visible-human [23]. Similar undertakings in Korea and China have resulted in the Visible Korean Human Project (http://vkh.ajou.ac.kr/) and the Visible Chinese Human Project (http://www.chinesevisiblehuman.com/index.htm) [36]. The Chinese and Korean projects are more recent than the Visible Human Project so voxel models have yet to be made from these data sets.

When cadavers are used it may not be possible to place the arms and legs as desired (see for example UF2 and BABY). In the case of VIP-man, the arms are crossed over the abdomen. Individuals may differ from the average height and mass. The Visible Human Project male was tall (186 cm) and heavy (104 kg). Furthermore, cadavers and individual subjects examined for diagnostic purposes may possess pathologies or significant changes from healthy anatomy. In the case of UF2, the subject was 6 months old, but being premature, was the size of a 2-month-old child. The lungs had partially collapsed and the results of a failed surgical procedure on the heart operation distorted the anatomy in that region.

Magnetic resonance imaging has been used to image volunteers for the express purpose of producing a whole-body voxel model [14, 32, 37]. In this case, the pixel size and slice interval may be selected as desired. However, the time required to MRI the whole body is long—8 h in the case of the Nagaoka models—and this allows subject movement and the heart beats to degrade the images. A drawback of MRI is that bone (ribs) may not be imaged adequately so some manual editing may be required [30].

## Voxel models may comprise images from more than one individual

In the case where a sequence of clinical images does not span the entire body, or when some images are unsuitable, it is possible to use a complementary series of images from an examination of a different individual—scaled to a different size if necessary—to construct a composite model. By this method, it is possible that different parts of the model have different $z$ resolutions (slice thickness). VoxelMan was originally a head and torso without arms and lower legs made from images separated by 10 mm. However it is available as a version known as VOXTISS8 which has been constructed from three individuals. VOXTISS8 has the arms (now uncrossed and placed alongside the body) and legs of the male from the Visible Human Project. It also has a new head which was scaled down from the MR images (slice thickness of 1.5 mm) of a 35-year-old male volunteer (see the VoxelMan website http://noodle.med.yale.edu/zubal/index.html). MAX consists of data from the same three individuals as VOXTISS8 but has had the arms and legs scaled to a smaller size so that they more accurately match the size of the VoxelMan body.

UF newborn had lungs of a similar size segmented from a CT examination of a live patient inserted in place of its own collapsed lungs [38]. Donna and Irene have the intestines from another female CT scan fitted into their pelvis [17]. While Donna and Irene had CT slice separations of 10 mm and 5 mm, respectively, the new abdomen had a slice thickness of 1.25 mm. Fill et al. segmented the new digestive system from a series of 300 slices from a barium enema contrast examination and adjusted it to fit into the existing voxel models and to conform to the organ masses of ICRP Report 23 [11].

## The construction of voxel models

The construction of tomographic models requires the identification of the boundaries between all the different organs and tissues that are displayed in a medical image. All the pixels belonging to an organ or tissue are assigned an organ identification number that replaces their original gray scale value. In this way every pixel that belongs to an organ or tissue may be identified and distinguished from pixels belonging to other organs. This process is known as segmentation, as the image is literally divided into smaller segments.

Segmentation is very time consuming because there are a great many boundaries and, for a series of images that span the whole body, there are a great many image files to process. The segmentation process is not straightforward as the boundaries between some structures are indistinct. For example using CT images, it is difficult to visualise the ovaries, the pancreas, the oesophagus and to distinguish the adrenal glands from the kidneys. Furthermore, the walls of hollow organs such as the intestines are not always discernable from their contents. Consequently, manual manipulation of the images using image-processing software and considerable anatomical expertise is required. This makes the segmentation task very time consuming—a fact that has been commented upon by several authors: "After primary segmentation by Fairfield Imaging, a further 6 months of the author's time was spent 'fine-tuning' the phantom." [30]; "It is very laborious work to (perform these) procedures manually." [39]; "...the development of these models took over three years." [32].

The long time and anatomical knowledge required to segment medical images has stimulated the development of interactive or semi-automatic segmentation techniques [40]. These techniques involve the use of existing image processing software or software specifically developed for the purpose of segmenting medical images [41]. Gray level CT and MR images provide very high resolution pictures that allow the expert to distinguish anatomical structures quite easily. However, completely automatic segmentation remains an unsolved problem. In a CT image, the pixels within an organ span a range of gray level values. Usually, the range of gray level values of one soft tissue organ, overlap those of adjacent organs. The lack of distinct differences between the pixel gray level ranges of organs makes the process of identifying boundaries of necessity an interactive one. Some organ boundaries have to be drawn manually. Nevertheless where air spaces and bones occur, the contrast is high and the opportunity for automating the segmentation process exists. A degree of automation was used to construct some of the existing voxel models: for example Otoko [20, 39], Golem [42], the 2 UF models [38], Donna, Helga and Irene [17]. The interested reader is directed to the cited articles for a detailed description of the methods adopted.

## The benefits of using voxel models

Voxel models are the most faithful representation of human anatomy currently available as they are designed from real anatomy—in fact the actual anatomy of an individual human. The MIRD models that they seek to supplant were designed as reference individuals whose organs had masses and volumes that were consistent with the model's size. Despite their lack of anatomical realism, these reference individuals have been used to provide consistent and reproducible radiation protection guidance for different types of exposure [3]. Voxel models exist that are a very good match for the height (176 cm) and weight (73 kg) of the Reference Man. Golem is 176 cm tall and weighs 70 kg, MAX is 175 cm tall and weighs 75 kg and NORMAN is 176 cm tall and 73 kg. Hence these models can be used for the same purposes as the MIRD type models of Reference Man and have the added benefit of realistic organ shape and placement. For dosimetry of internal radionuclides, the masses of those organs involved in the metabolism of a radionuclide are of importance [29]. Therefore individual deviations from the reference organ masses need to be considered when interpreting results obtained from an individual voxel model. By being subjected to the same irradiation conditions, the three models above could be used to estimate the amount of variation in organ dose that can be expected to arise due to variations in internal anatomy.

ICRP publication 89 goes on to say (page 7) "...retrospective dosimetry calculations and analyses for specific individuals in specific exposure situations should use values appropriate for the individuals involved when this information is available.". In other words, there are situations where a model with the dimensions of Reference Man is not the most suitable to use. The dimensions of Reference Man are based on data from western Europeans and North Americans obtained in the 1970s and 1980s. For dosimetry applicable to Asian people, the voxel models now available for Japanese and Korean individuals (Table 1) are more suitable than (European) Reference Man. A review of anthropometric data for USA people measured between 1971 and 2000, found a large number of overweight people (body mass index greater than 25) [43]. The present US 40-year-old male was 16% heavier than Reference Man. They also found that the 73 kg/176 cm hermaphrodite MIRD style model more closely resembled adult US females between 20 and 70 years of age, than did the 60 kg/163 cm reference weight and height for the MIRD model female. As a consequence of the increasing number of overweight people, the MIRD models that are based on Reference Man data do not reflect the present average sizes of USA residents.

When a more extensive range of voxel models that vary in age, gender, ethnicity, size and height become available, they will allow a close match between a model and an individual patient to be made. Where a voxel model exists that is close to but different in size from an individual patient, the model can be "scaled" by altering the dimensions of its voxels [44, 45]. In fact both

NORMAN and MAX were scaled during construction to match the dimensions of Reference Man. ADELAIDE has been decreased and increased in size to represent girls aged between 11 and 16 years old in order to calculate organ doses from CT [19]. In this way a voxel model may be made to more closely resemble an individual patient.

## Shortcomings of voxel models

The characterisation of 3D volumes as made up of voxels has produced far more realistic representations of human anatomy than was possible when equations were used. Nevertheless, voxel models are not without their limitations. Structures having dimensions less than the dimensions of the voxels cannot be accurately segmented. For example the skin thickness is defined by the side length of a pixel and this may result in a skin thickness and mass that is too large. To some extent this shortcoming may be overcome during dosimetry calculations by coding the radiation transport to assign energy deposited in only the first 1.5 mm of a skin voxel to skin [24]. Also "bone surface" (periosteum), a tissue to which absorbed dose must be estimated in order to determine effective dose [46], is too thin to be represented by a voxel. In this case, another tissue is used as a surrogate in order to calculate effective dose. Neither voxel models nor MIRD models adequately represent the bone surface.

Being composed of voxels, the surface of an organ has a "stepped" nature rather than being a smooth surface. This will have the effect of overestimating the surface area of an organ [47], particularly those with approximately spherical shapes. The effect on organ dose calculations of stepped surfaces for organs rather than smooth surfaces, may not be large. Jones compared specific absorbed fractions calculated with a MIRD model and a voxel version of the same model when an internal gamma emitter was located in the stomach [25]. He found that there was generally good agreement between the values. Zankl [4] cited results from a previous work [48] (written in German) where the measured dose in dosemeter capsules placed in an Alderson-Rando phantom were in good agreement with the Monte Carlo calculated doses in a voxel model of the phantom.

Medical images from extensive CT scans and MRI are usually acquired from patients that are supine. Consequently the weight bearing surfaces are somewhat flattened [30], the abdominal cross-section is influenced by the force of gravity acting towards the dorsal surface rather than towards the feet. Furthermore the internal organs are shifted by gravity to positions different from those that the organs would adopt if the subject had been standing [42]. While the supine position is required for the calculation of doses from CT examination, when a standing person is to be simulated by a voxel model, the altered organ positions may need to be considered.

Voxel models, being constructed from the images obtained from an individual, may differ significantly in their internal anatomy from that of another individual of similar size. Consequently, when one model is used for the calculation of estimated organ doses to an individual patient, the results must be interpreted with due care. When several voxel models of about the same size become available and Monte Carlo calculations of the organ doses received from the same irradiation conditions are made, some limits to the uncertainty in organ doses associated with individual variations in internal anatomy can be made. However this shortcoming of computational models is even greater for the MIRD models.

Segmentation of images is laborious and involves many steps and the use of judgement. Consequently the process may be imperfect and is subject to error. Images from the same individual when segmented by different workers may give rise to different organ masses [23]. In this case (the Visible Human Project male) the Zankl et al. Visible-human was segmented from CT images while VIP-man of Xu et al. [35] was segmented from photographic images. The discrepancies may be as little as 5% (for liver), to 24% (for oesophagus) and higher for small organs. It seems probable that without higher resolution images, the uncertainties associated with organ masses will be of the order of 10% or more. When Kramer et al. revisited the segmentation of VoxelMan during their construction of MAX, they found significant errors in the original segmentation [24]. It can be expected that the reproducibility of segmentation will improve as automatic segmentation techniques improve. However for small organs and organs that are difficult to distinguish in medical images, the requirement on the part of the segmenter for the use of judgement will ensure that some subjectivity will persist.

## Conclusion

Descriptions of 10 adult male (from 8 individuals) and 5 adult female voxel tomographic models have appeared in the literature. In addition, voxel models of 6 children exist. These voxel models have been used for dosimetry purposes in radiography, nuclear medicine, radiation protection, radiotherapy and with low frequency electromagnetic fields. It is likely that more voxel models will be produced in the near future when data sets presently being segmented are completed, as additional data sets become available, and as semi-automatic segmentation techniques become more sophisticated. These computational models approximate real human anatomy more realistically than the MIRD-style mathematical models. Some of the male voxel models have height and weight very similar to those of Reference Man and could be used for the same purposes as a mathematical model of Reference Man and are expected to produce more accurate results. Voxel models have the flexibility of being able to be scaled by small amounts to more closely match the individual being investigated or suit the purpose to which they are put.

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