An Image-Based Canine Phantom for Pre-Clinical Evaluations of Osteosarcoma Molecular Radiotherapy

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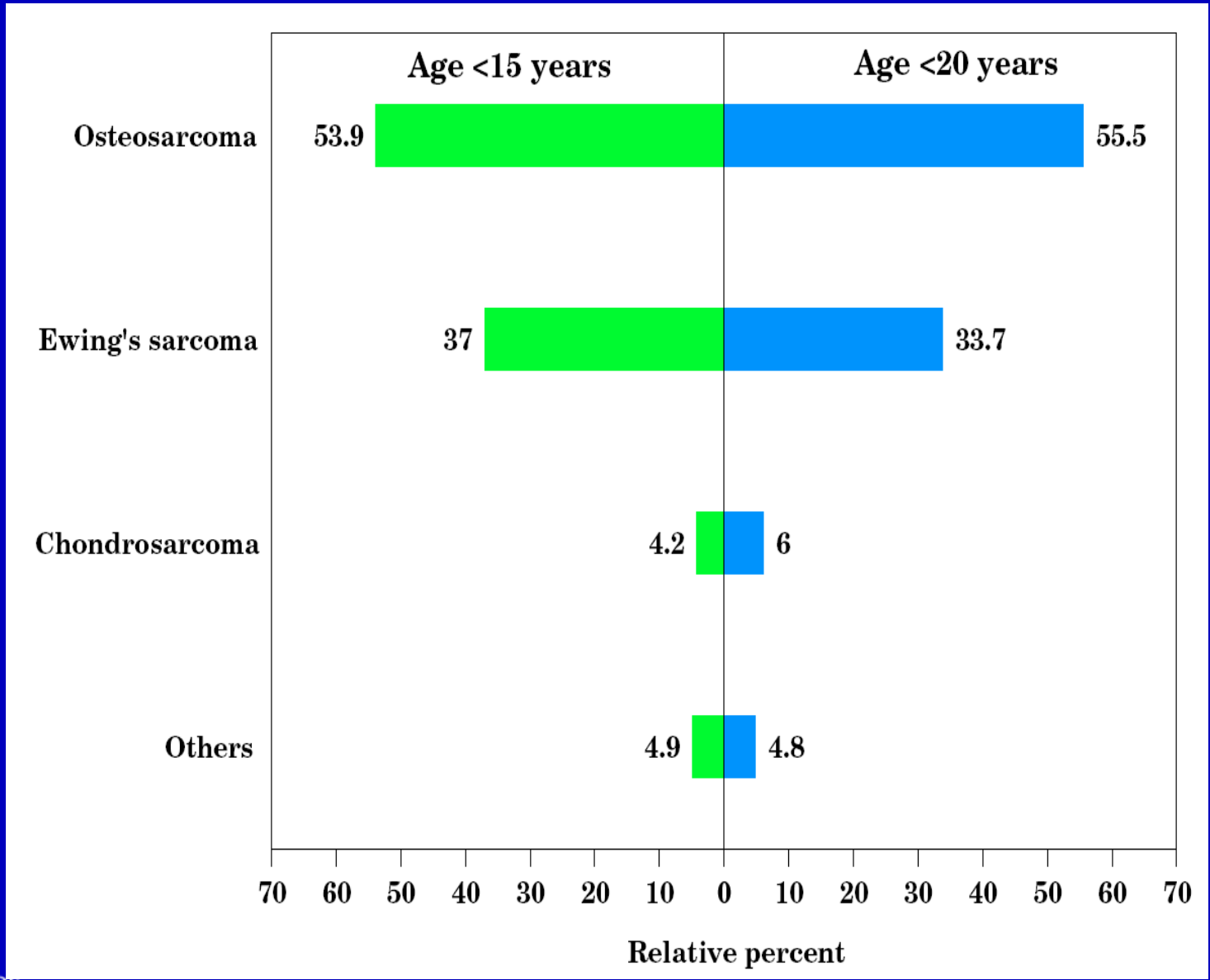
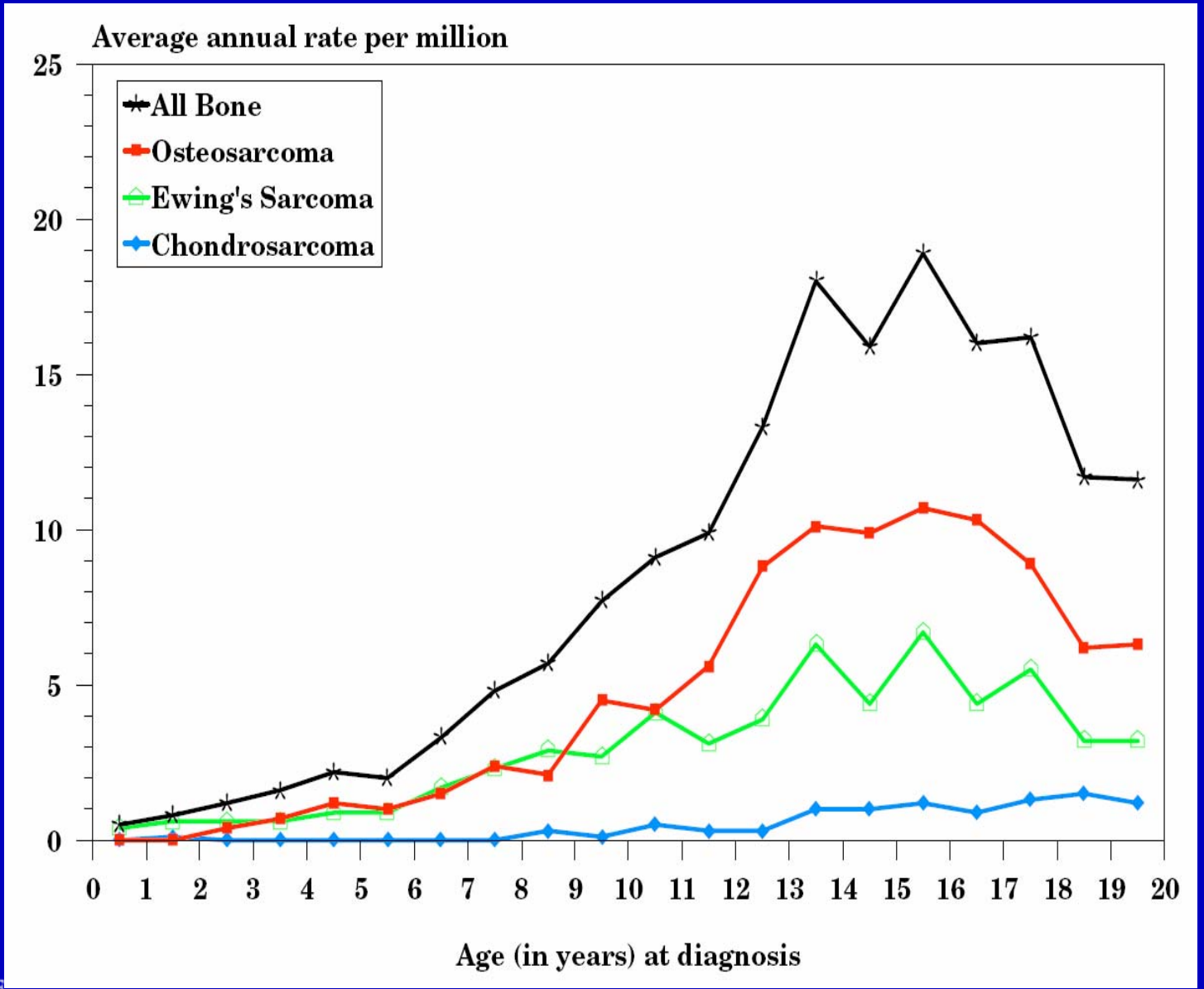
Pediatric Bone Cancers

- ***Osteosarcoma***
  - ⇨ Malignant tumor of the connective tissues (*sarcoma*) of bone (*osteo*)
  - ⇨ Cells involved: mesenchymal stem cells of bone marrow
  - ⇨ Sites involved: metaphyseal portions of the long bone (growth plates)
  - ⇨ Approximately 400 cases per year / children < 20 years (63% survival)
- ***Ewing's sarcoma***
  - ⇨ Also called primitive neuroectodermal tumours (PNET)
  - ⇨ Cell involved: Neuroectoderm – embryonic tissues than develop to brain, spinal cord, and nervous tissues of the peripheral NS
  - ⇨ Sites involved: evenly between extremities and the axial skeleton
  - ⇨ Approximately 200 cases per year for children < 20 years
- ***Chondosarcoma***
  - ⇨ Malignant tumor derived from the cartilage cells of bone

Pediatric Bone Cancers



Pediatric Bone Cancers



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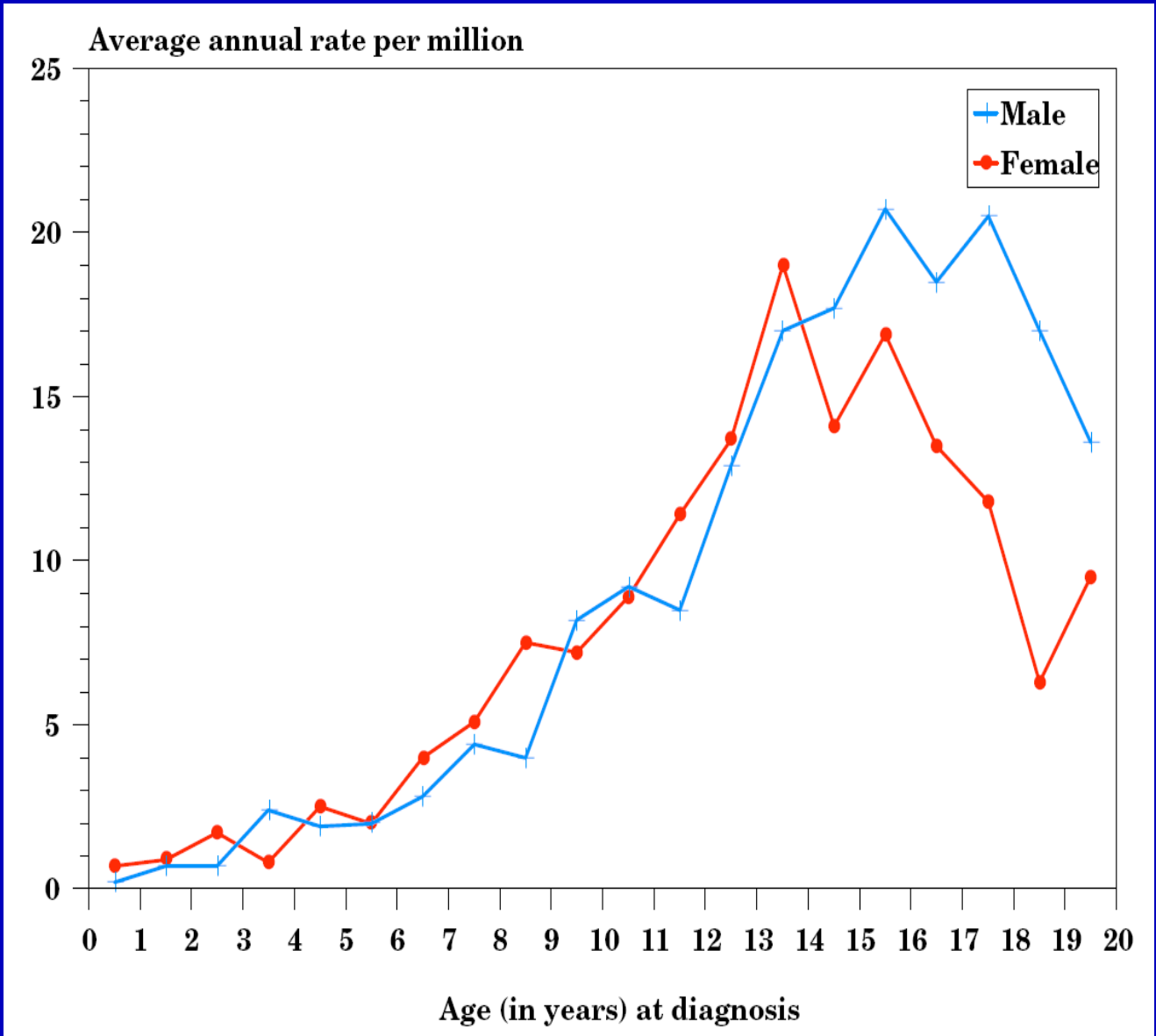
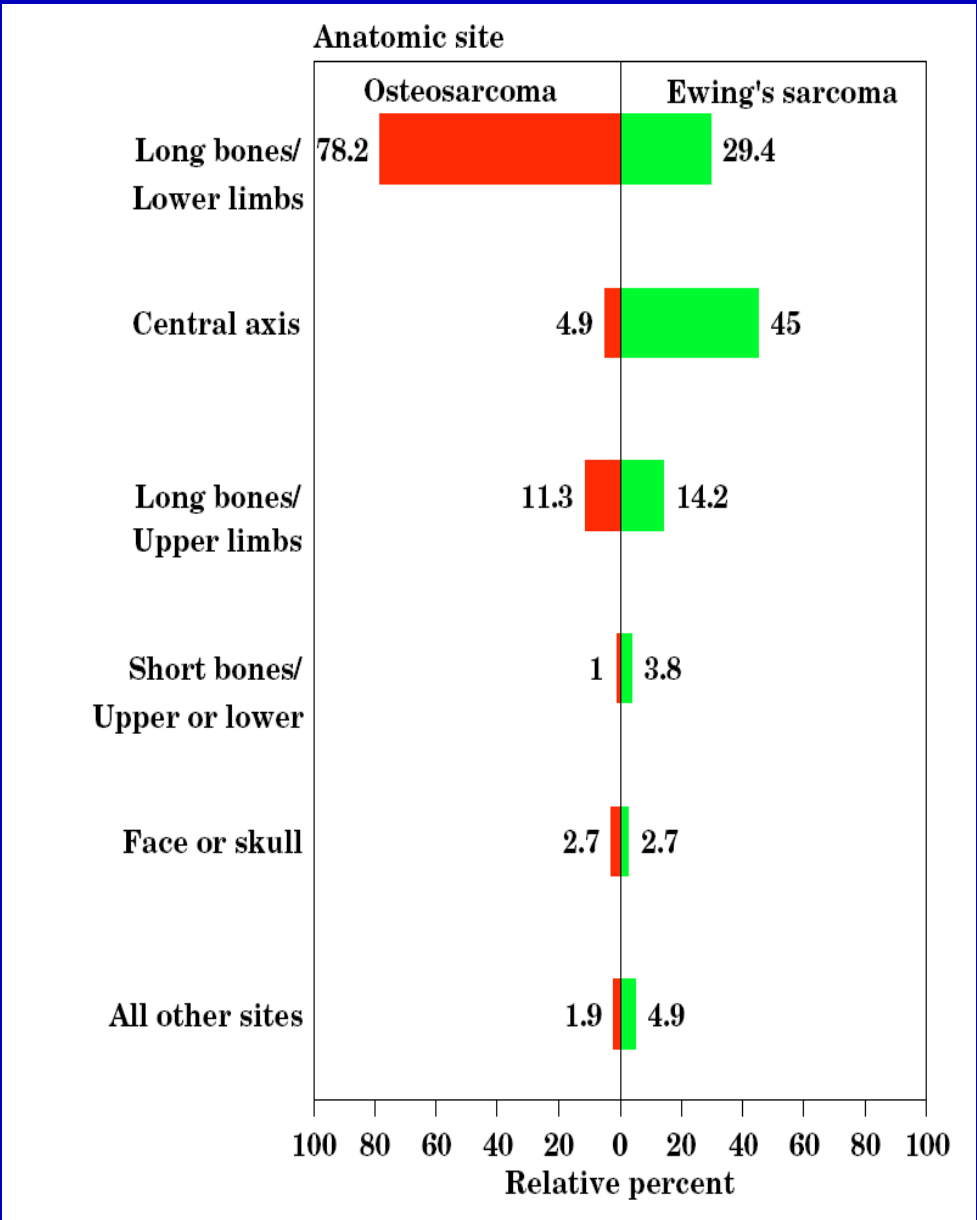


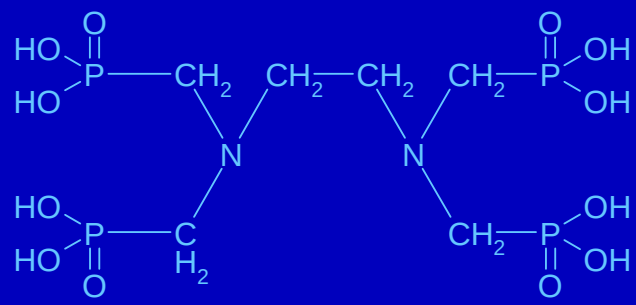
Pediatric Bone Cancers



Treatment Options

- ***Surgery*** *(including amputation)*
- ***Chemotherapy***
- ***External beam radiotherapy (> 70 Gy)***
- ***Molecular radiotherapy***
  - ⇨ ***Sm-153 EDTMP***
  - ⇨ ***Covalent bond with Sm***
  - ⇨ ***Interfers with osteoclasts***
  - ⇨ ***Incorporates within hydroxyapatite crystals***

EDTMP



Preclinical Studies of Radiopharmaceuticals

- ***Murine model – mice***
  - ⇨ Positives: available, short lifespan, genome well established
  - ⇨ Negatives: skeletal system very small relative to human dimensions
- ***Primate model – baboons***
  - ⇨ Positives: extremely close to skeletal structure of humans
  - ⇨ Negatives: limited availability and very expensive
- ***Canine model – dogs***
  - ⇨ Positives: large population available (4 million cancers / year)
  - ⇨ Postives: canine genome recently established
  - ⇨ Postives: many histological and biochemical similarities in disease
  - ⇨ Negatives: not many – lack of a dosimetry phantom!

AACR 2006

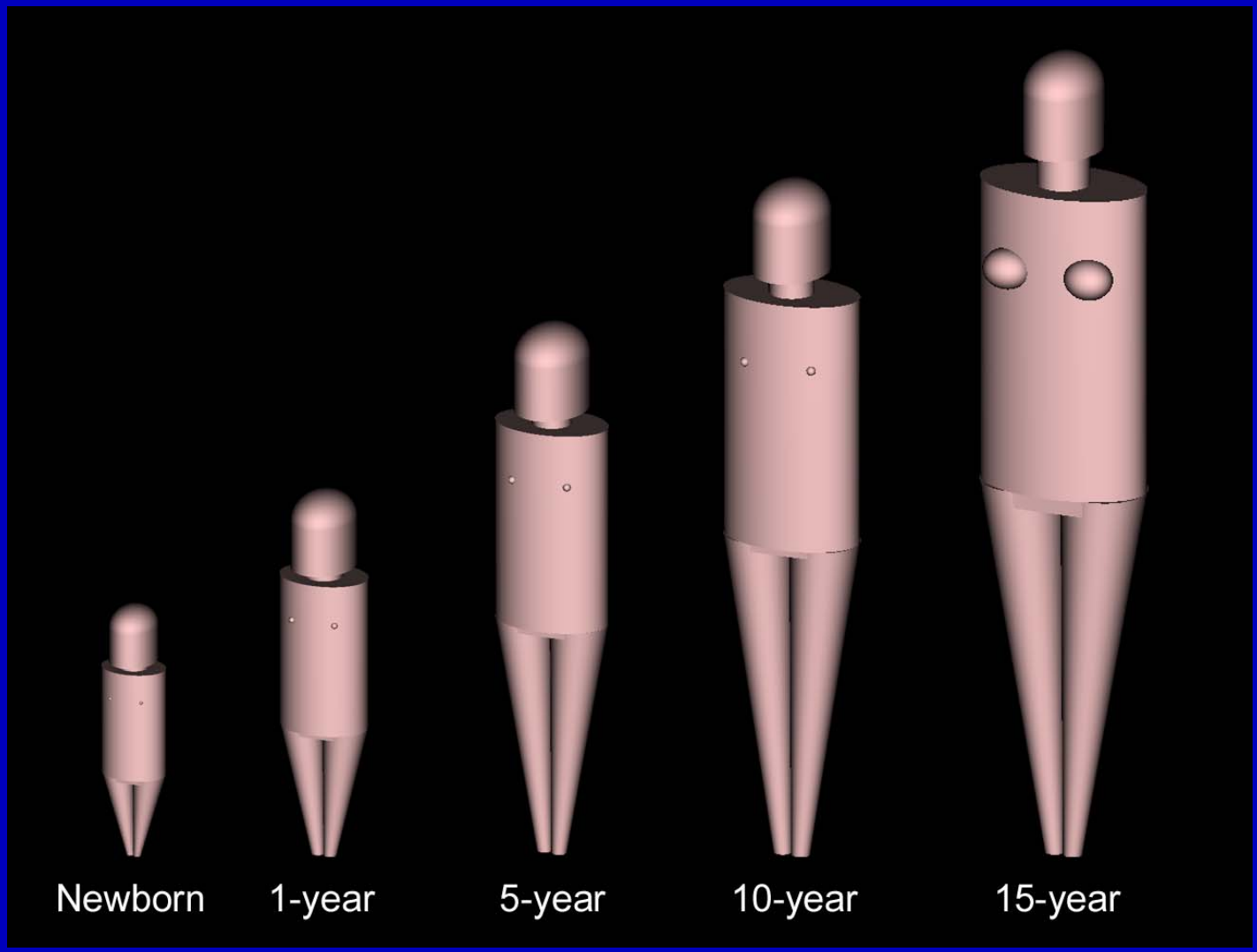
Comparative gene expression analysis of canine and human osteosarcoma *Paoloni et al.* NIH

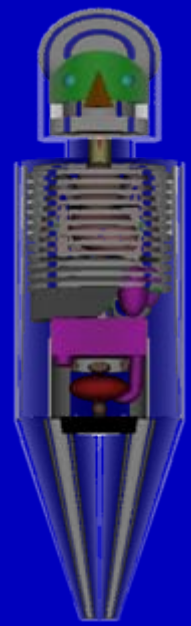
- "Tumors from both species were co-mingled within a single osteosarcoma cluster."

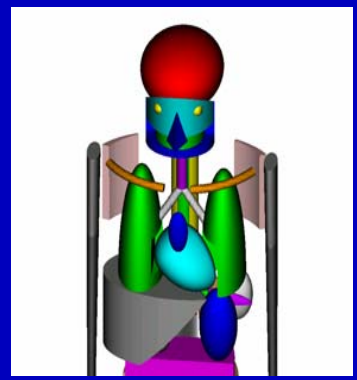
- "This data provides strong genomic evidence of the similarity and relevance of canine osteosarcoma as model for the human disease."

Equation-Based Computational Phantoms

Oak Ridge National Laboratory (ORNL) Series

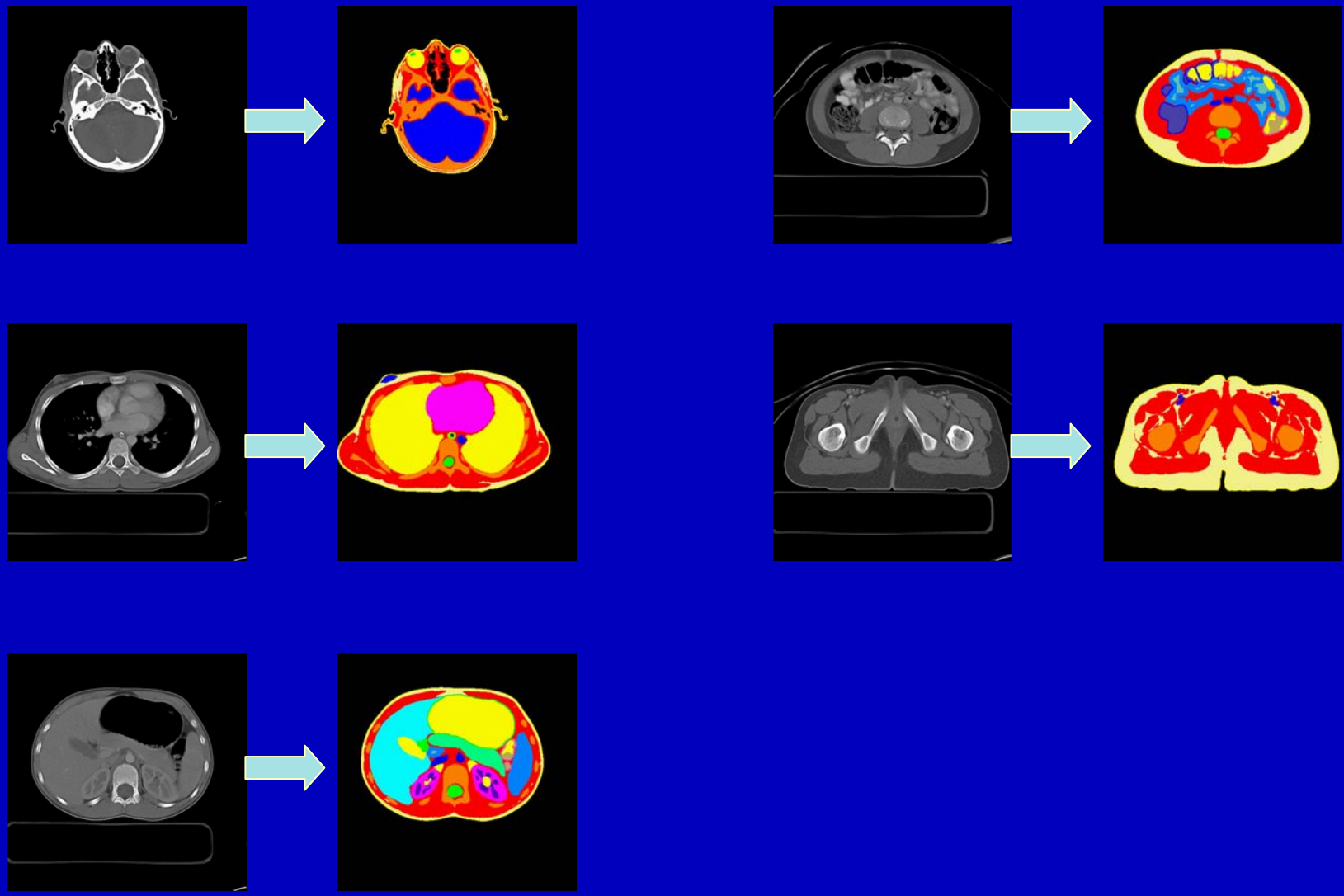






Voxel-Based Computational Phantoms

University of Florida (UF) Series



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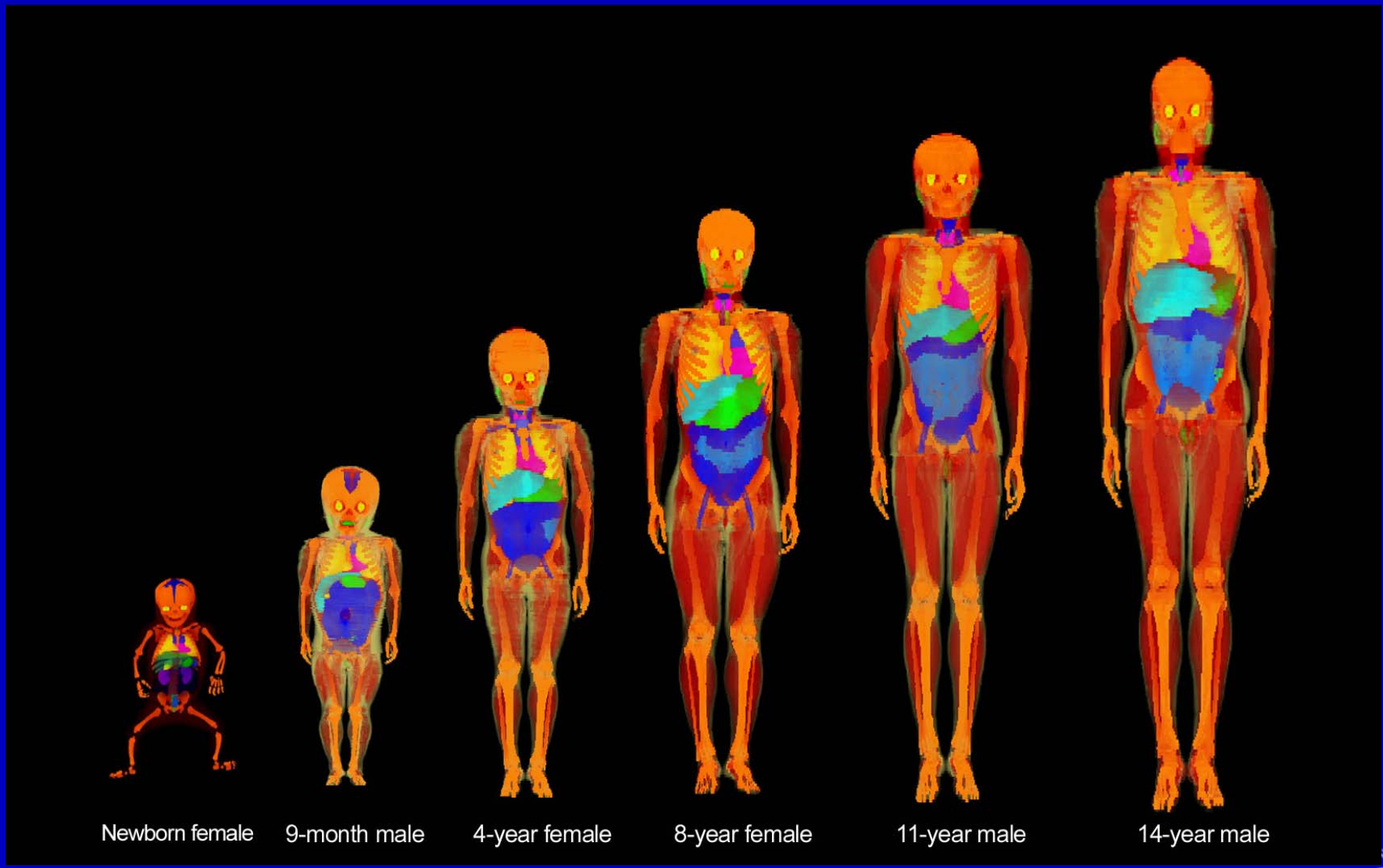

Hybrid Phantoms

Anatomic Realism (Voxel) with Scalability (Stylized)

IOP PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY

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Hybrid computational phantoms of the male and female newborn patient: NURBS-based whole-body models*

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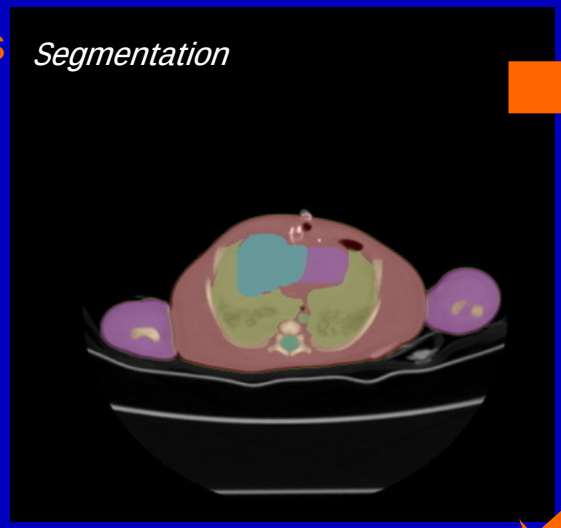
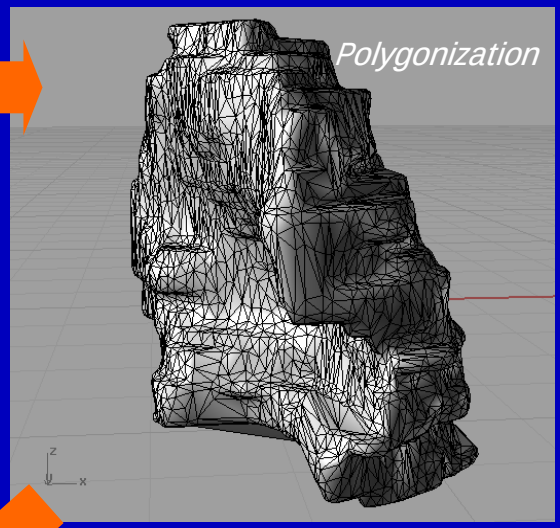
Abstract

Anthropomorphic computational phantoms are computer models of the human body for use in the evaluation of dose distributions resulting from either internal or external radiation sources. Currently, two classes of computational phantoms have been developed and widely utilized for organ dose assessment: (1) stylized phantoms and (2) voxel phantoms which describe the human anatomy via mathematical surface equations or 3D voxel matrices, respectively. Although stylized phantoms based on mathematical equations can be very

Procedure for hybrid phantoms

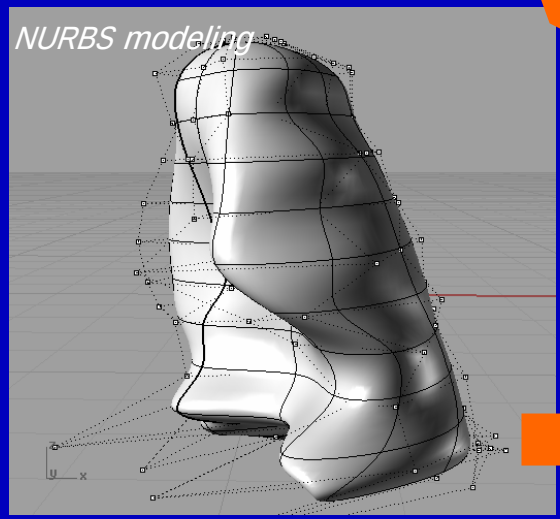
Segment CT slices using 3D-DOCTOR, 3D segmenting and rendering software

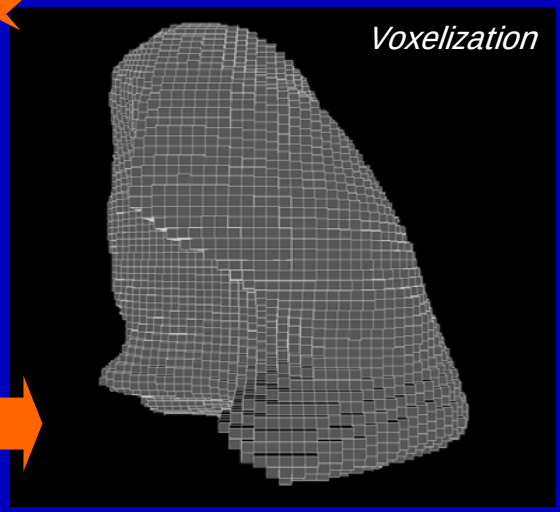




Convert segmented model into polygon mesh using built-in function of 3D-DOCTOR

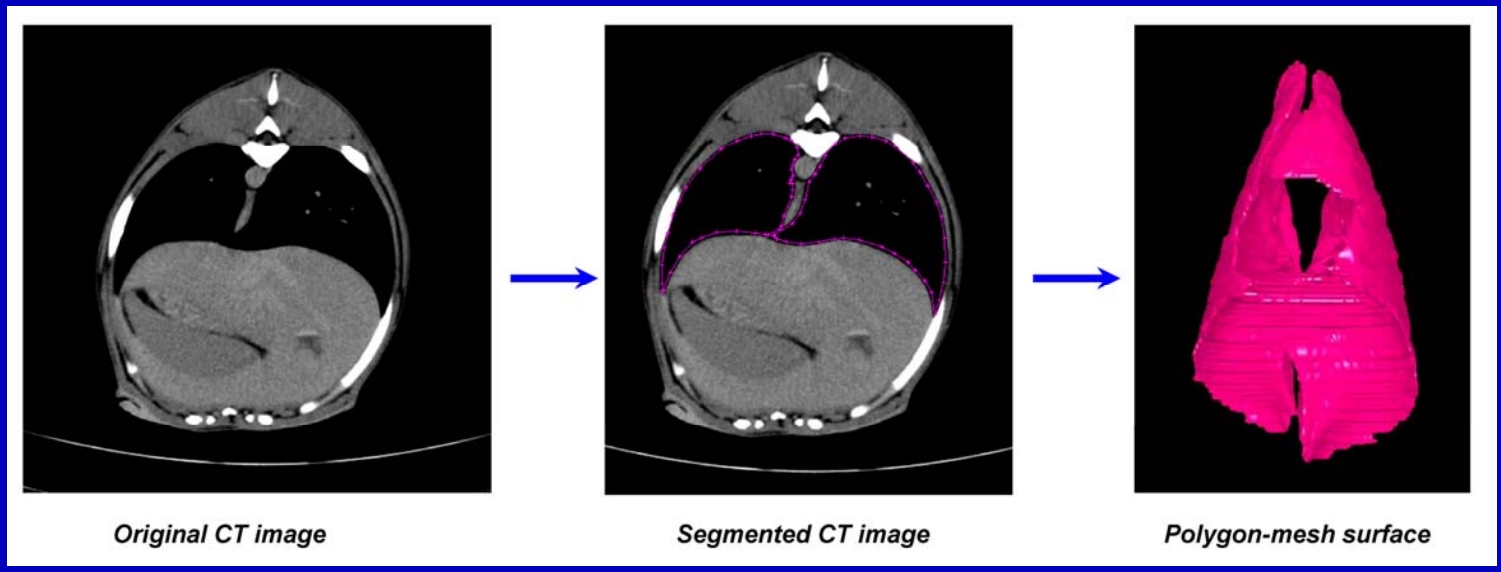
Make NURBS model from polygon mesh model using Rhinoceros, 3D NURBS modeling software, and match to ICRP89 reference organ mass

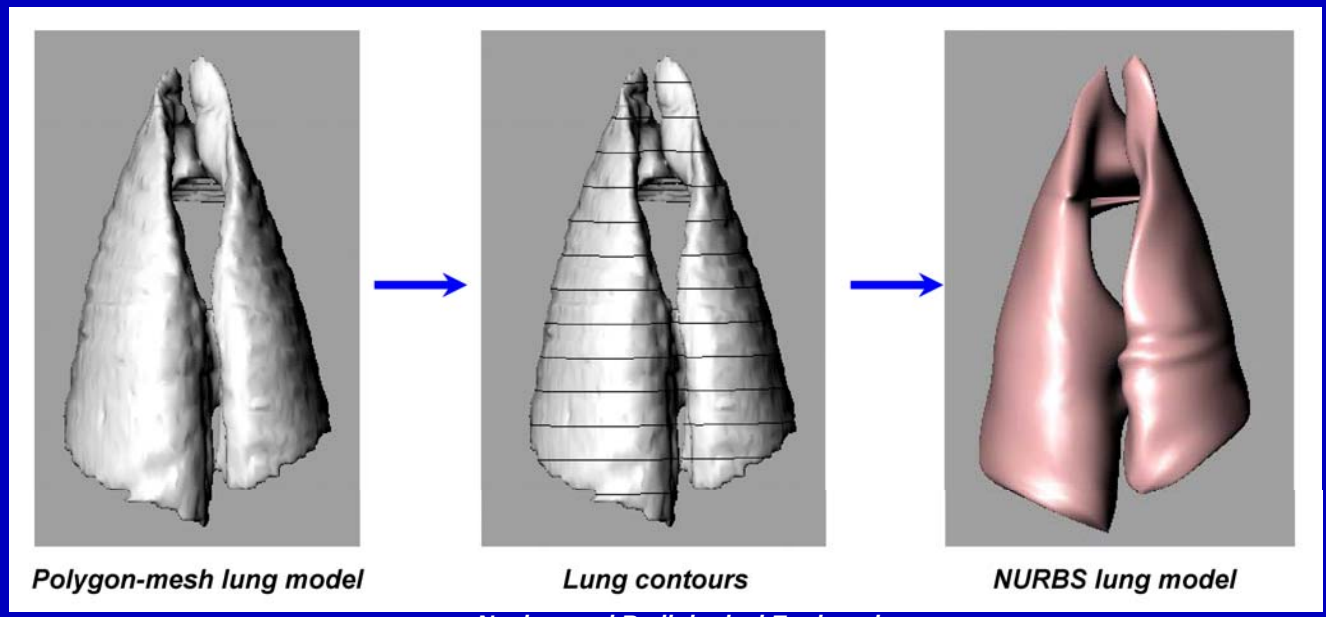




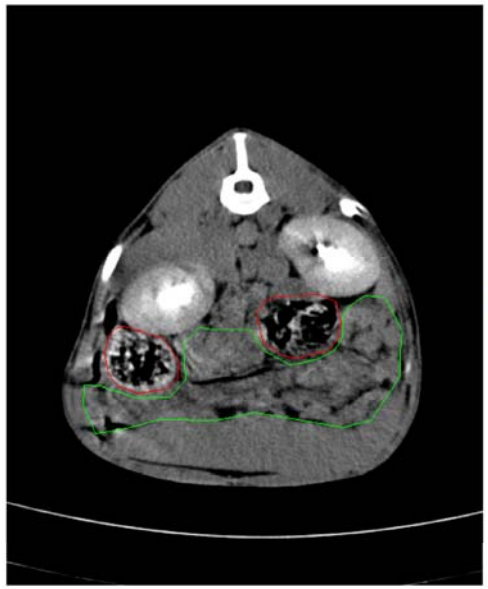
Convert NURBS model into voxel model using Voxelizer, in-house MATLAB code

Creation of the NURBS Lung Model

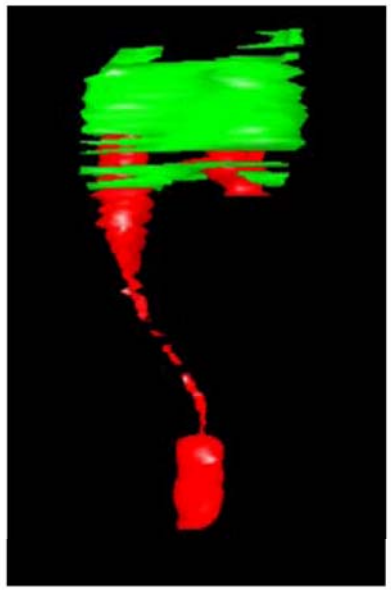




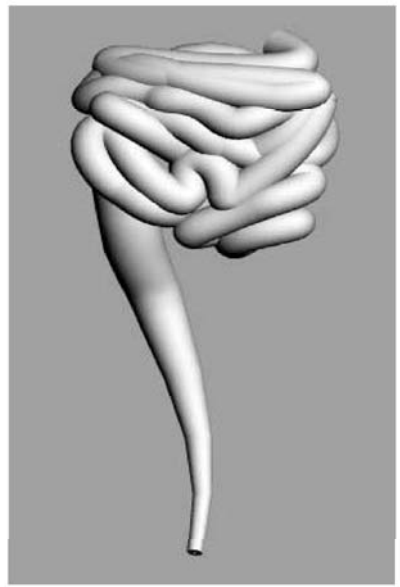
Creation of the NURBS GI Tract Model



Intestinal Area Segmentation

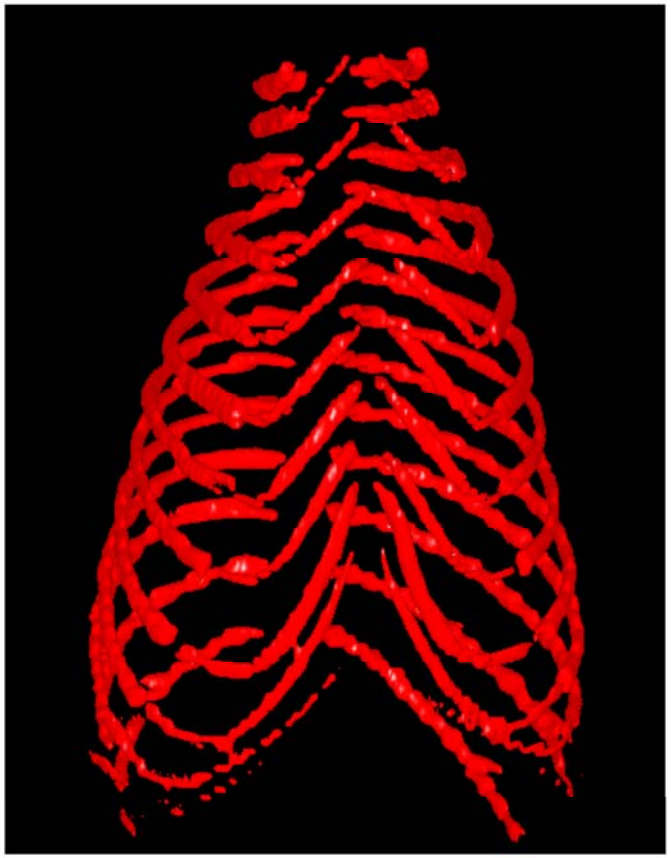


Intestines within 3D Doctor

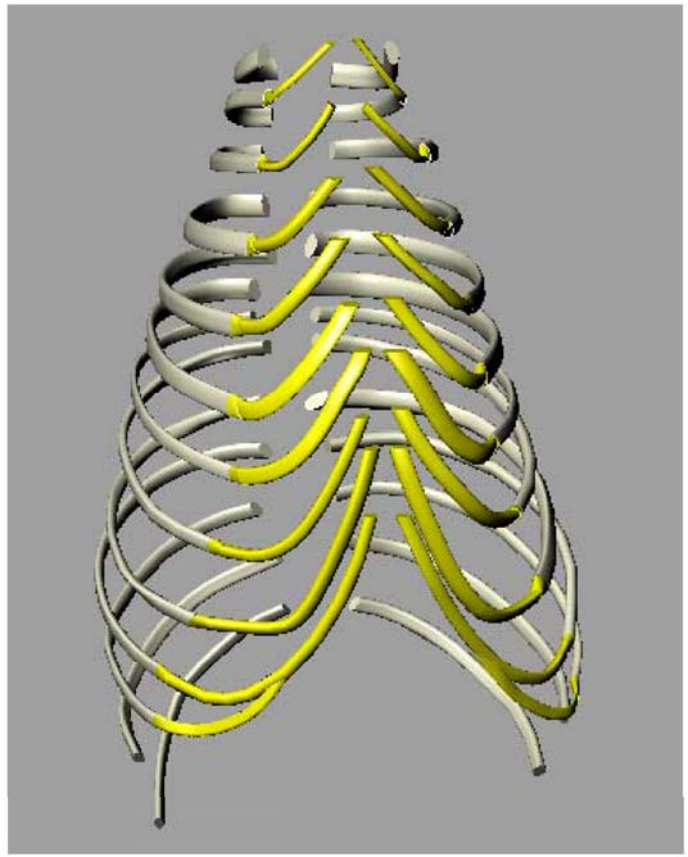


Intestines within Rhinoceros

Creation of the NURBS Rib Cage Model

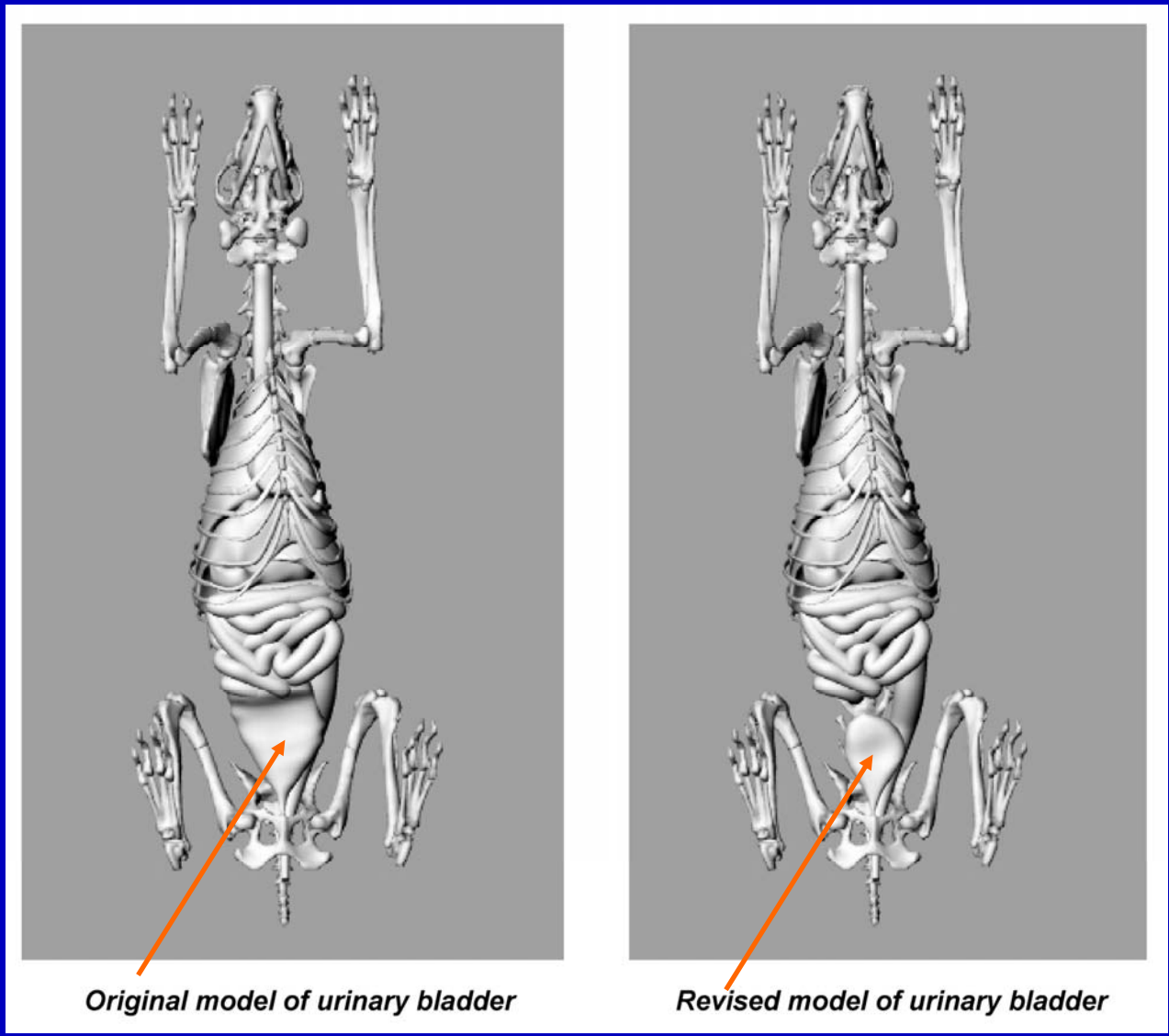


Polygon-mesh model of the ribs

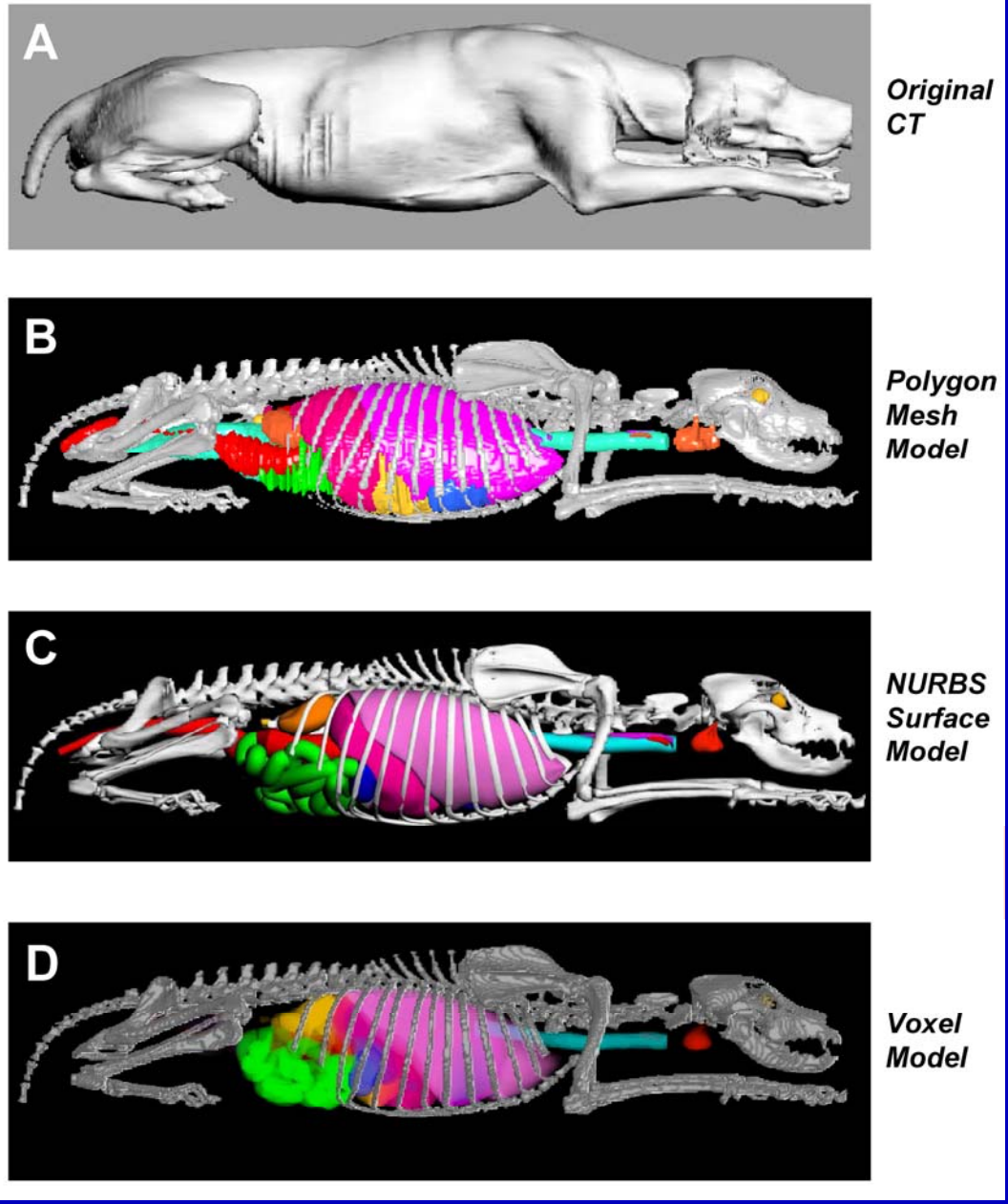


NURBS surface model of the ribs

Adjustment of Urinary Bladder Model



Final NURBS Hybrid Canine Phantom



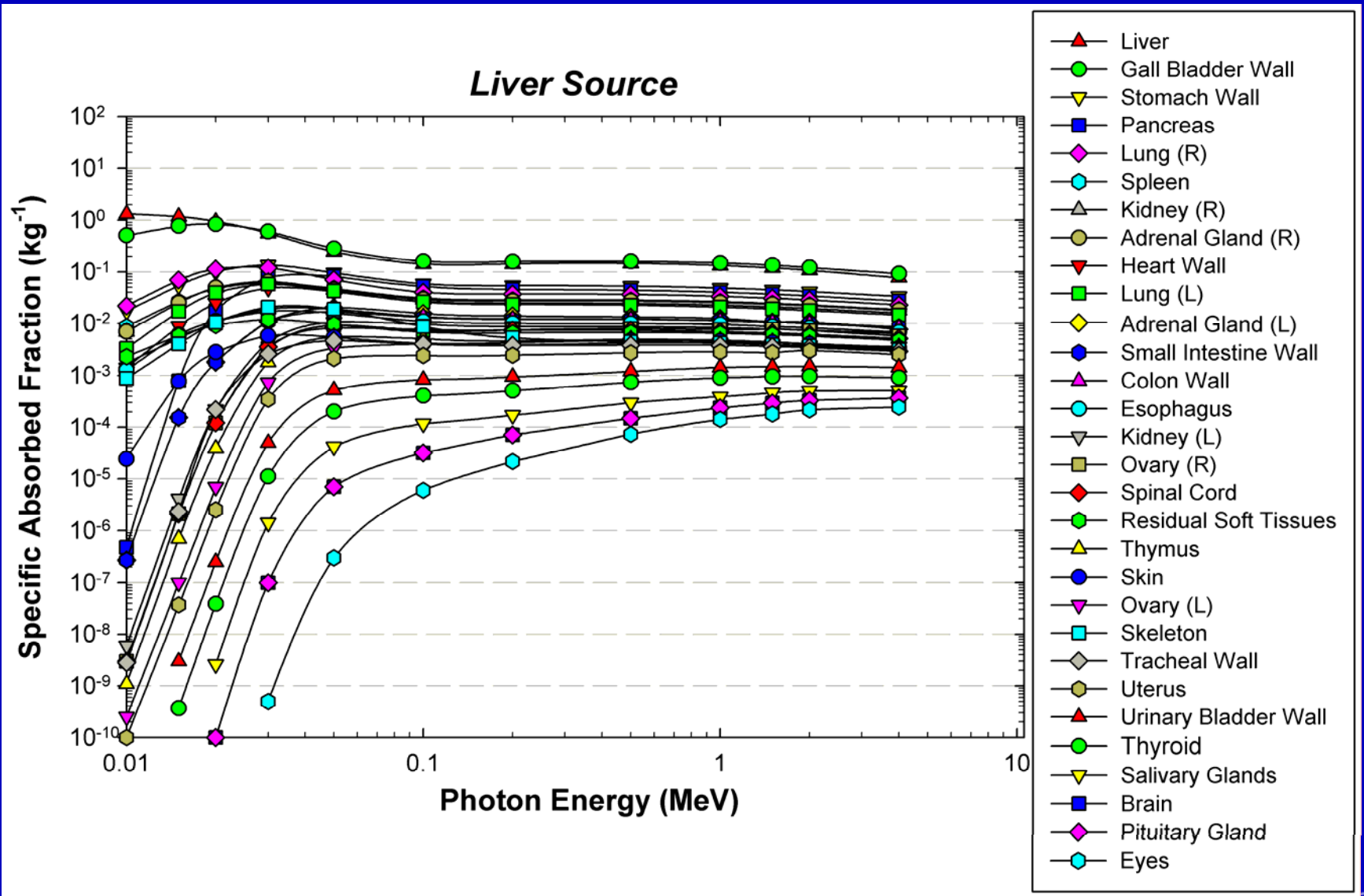
Final Tissue Masses

Organ System	Density (g/cm^3)	Organ Volume (cm^3)	Organ Mass (g)
Respiratory System			
Trachea - wall	1.04	37.51	39.01
Lung (Left)	0.296	630.81	186.72
Lung (Right)	0.296	1119.54	331.38
Totals:		*1787.86*	*557.11*
Alimentary System			
Salivary glands	1.04	30.36	31.57
Esophagus - wall	1.04	11.11	11.56
Stomach - wall	1.04	66.02	68.66
Stomach - contents	1.04	316.24	328.89
Small Intestine - wall	1.04	176.78	183.85
Small Intestine - contents	1.04	494.64	514.43
Colon - wall	1.04	180.26	187.47
Colon - contents	1.04	296.79	308.66
Liver	1.04	680.58	707.80
Gall Bladder - wall	1.04	1.01	1.05
Gall Bladder - contents	1.04	5.98	6.22
Pancreas	1.04	1.83	1.91
Totals:		*2261.61*	*2352.07*
Circulatory System			
Heart - wall	1.04	170.97	177.81
Heart - content	1.04	236.85	246.32
Totals:		*407.82*	*424.13*
Urogenital System			
Kidney (Left)	1.04	98.05	101.97
Kidney (Right)	1.04	96.92	100.80
Urinary Bladder - wall	1.04	30.09	31.29
Urinary Bladder - contents	1.04	97.54	101.44
Ovary (Left)	1.04	1.384	1.44
Ovary (Right)	1.04	0.59	0.62
Uterus	1.04	3.976	4.14
Totals:		*328.54*	*341.69*
Integumentary System			
Skin	1.04	2000.04	2080.04

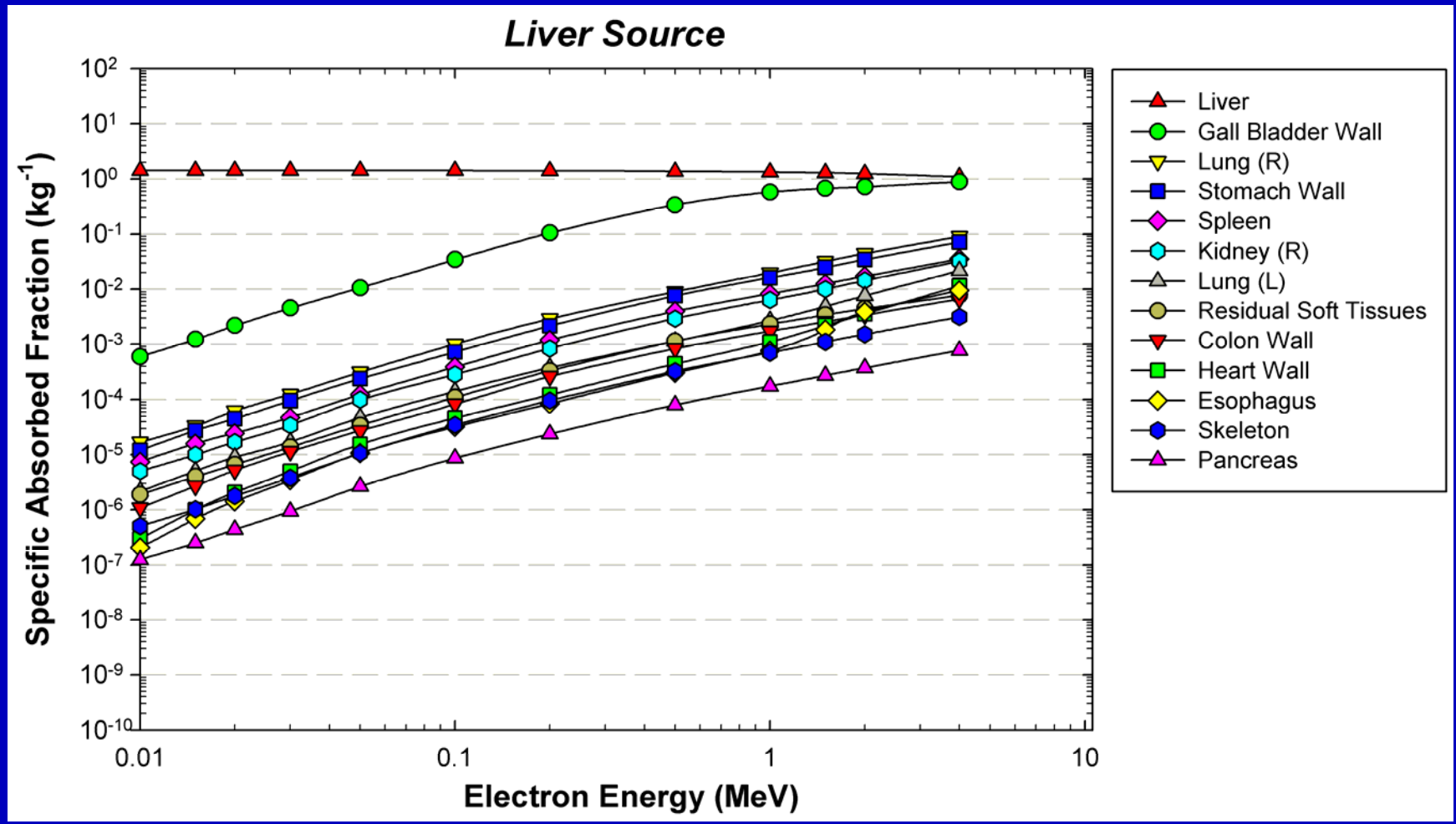
Organ System	Density (g/cm^3)	Organ Volume (cm^3)	Organ Mass (g)
Skeletal System			
Cranium	1.40	174.20	243.88
Mandible	1.40	82.11	114.96
Scapulae	1.40	99.50	139.29
Sternum	1.40	12.90	18.07
Ribs	1.40	113.77	159.28
Coastal cartilage	1.10	37.95	41.75
Vertebrae (cervical)	1.40	118.80	166.32
Vertebrae (thoracic)	1.40	129.84	181.78
Vertebrae (lumbar)	1.40	129.15	180.81
Sacrum	1.40	24.69	34.56
Vertebrae (caudal)	1.40	26.82	37.55
Os Coxae	1.40	105.19	147.27
Femur - upper half	1.40	80.56	112.78
Femur - lower half	1.40	82.40	115.36
Tibiae	1.40	112.44	157.42
Fibulae	1.40	8.46	11.85
Hind paw bones	1.40	53.29	74.60
Humerus - upper half	1.40	72.22	101.11
Humerus - lower half	1.40	73.02	102.22
Radii	1.40	62.81	87.93
Ulnae	1.40	53.66	75.13
Front paw bones	1.40	97.79	136.91
Totals:		*1751.58*	*2440.83*
Additional Tissues			
Air passages	0.0012	64.78	0.08
Adrenal Gland (Left)	1.04	0.18	0.19
Adrenal Gland (Right)	1.04	0.11	0.12
Brain	1.04	82.83	86.15
Eyes	1.04	9.36	9.73
Pituitary gland	1.04	0.016	0.02
Spinal cord	1.04	18.104	18.83
Spleen	1.04	362.37	376.86
Thymus	1.04	0.76	0.79
Thyroid	1.04	0.94	0.98
Residual Soft Tissues (RST)	1.04	16679.90	17347.09
Totals:		*17219.35*	*17840.84*

Total Body Tissues (kg)	24.5
Total Body Mass (kg)	26.0

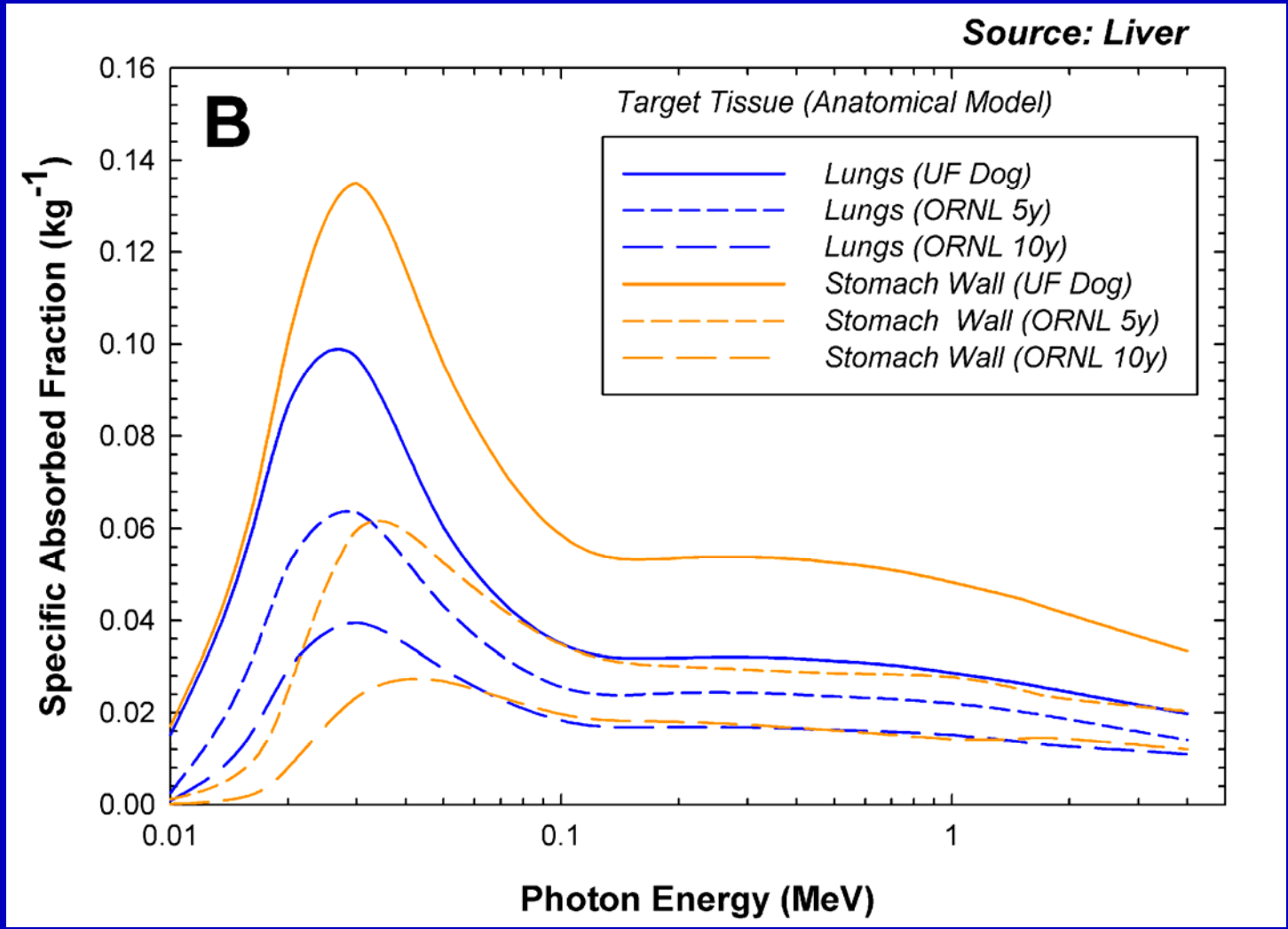
Recommended Values – Photon SAF



Recommended Values – Electron SAF



Comparisons with ORNL Phantoms



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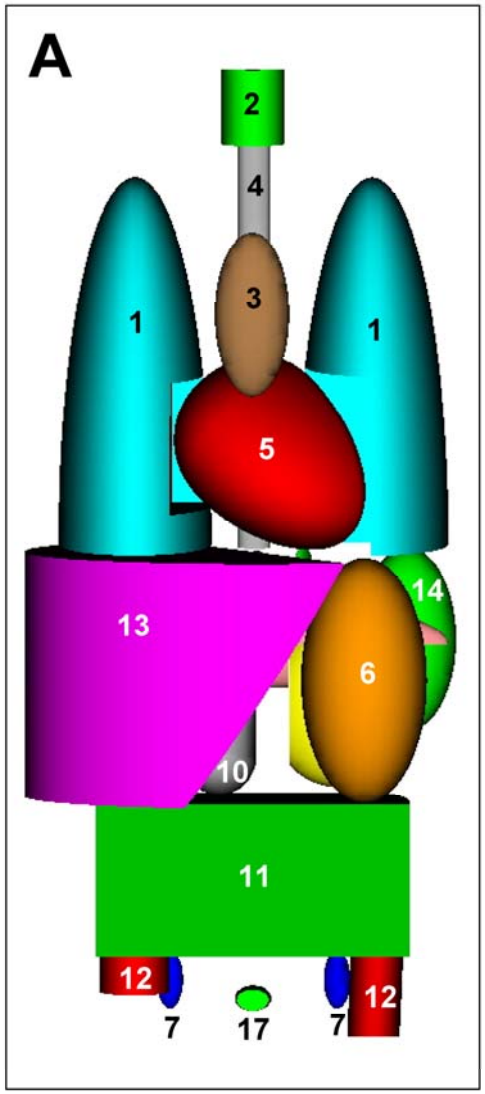
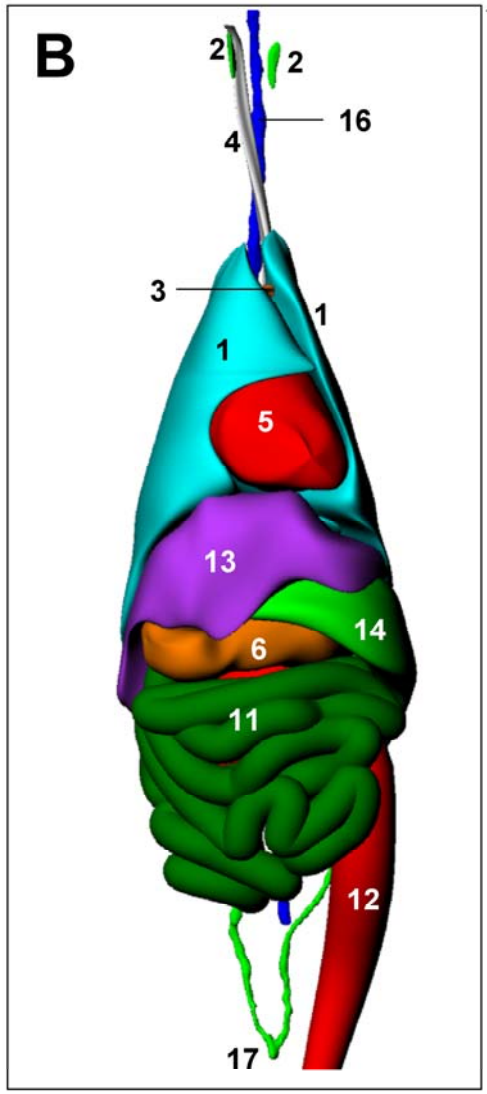
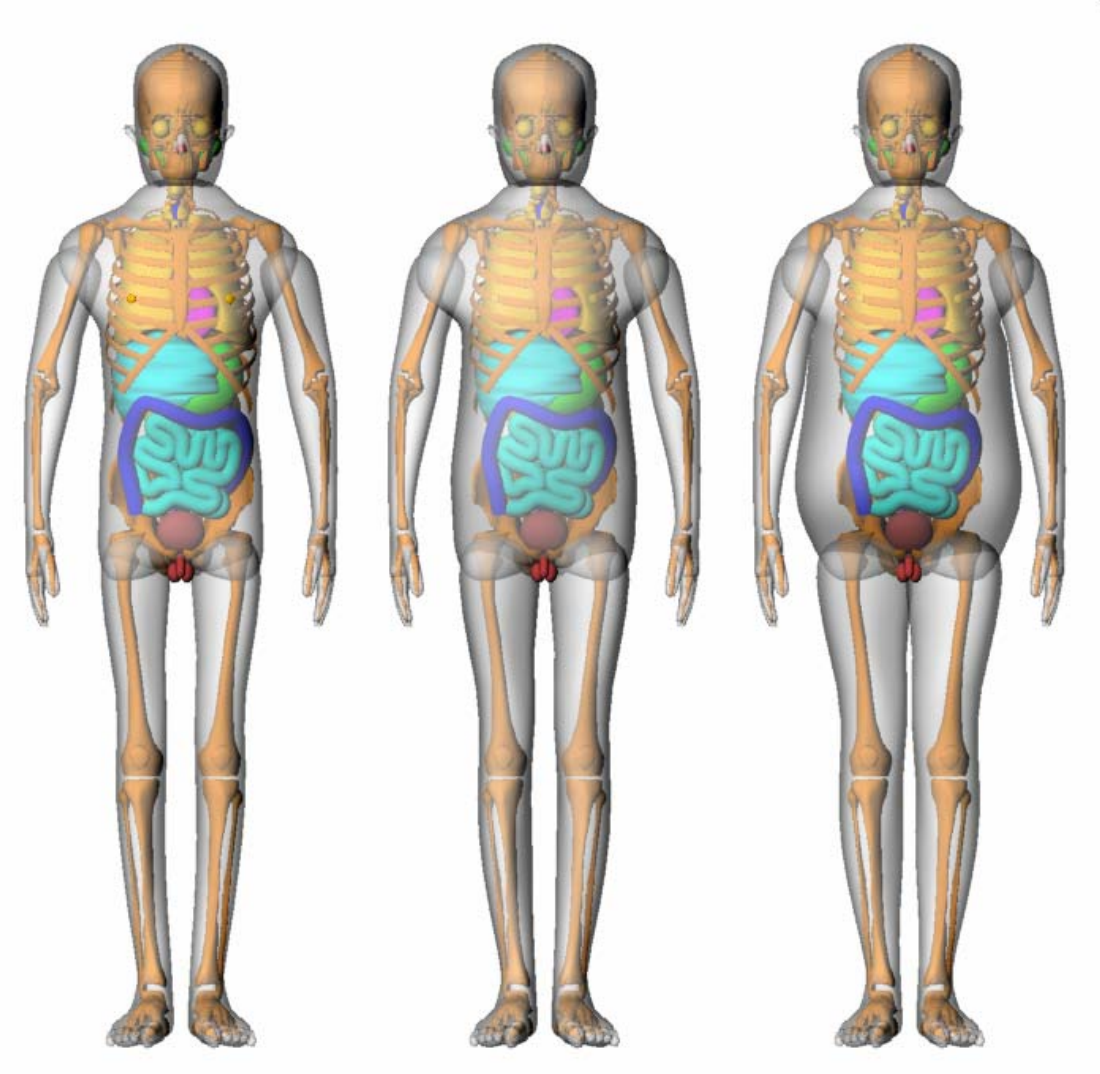




1. Lungs
2. Thyroid
3. Thymus
4. Esophagus
5. Heart
6. Stomach
7. Ovaries
8. Pancreas
9. Adrenal Glands
10. Gall Bladder
11. Small Intestine
12. Colon
13. Liver
14. Spleen
15. Kidneys
16. Spinal Cord
17. Uterus

Future Extensions to Human Hybrid Phantoms



Frontal views of 10th (left), 50th (center), and 90th (right) weight percentile hybrid 15-year phantoms

This concludes my presentation -

I would be happy to entertain any questions…