A Skeletal Reference Dosimetry Model for the Adult Female

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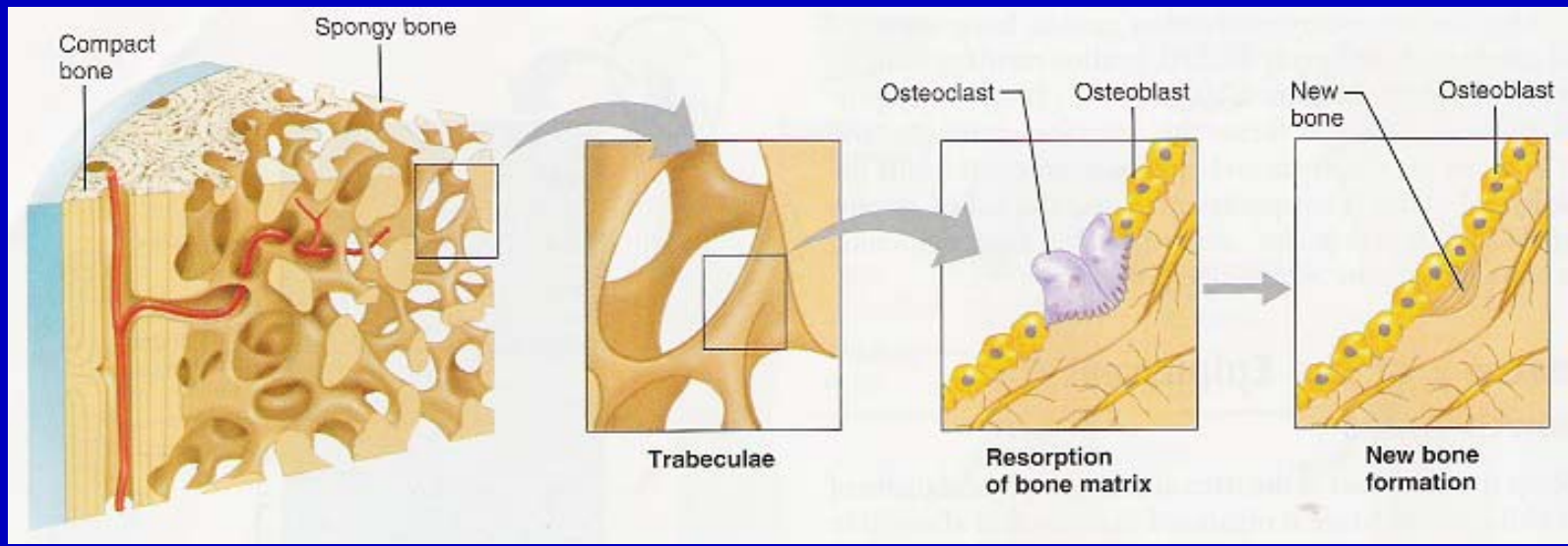
Introduction

- **In order to predict the risk of bone cancer, an accurate assessment of absorbed dose to skeletal tissues is necessary.**
- **Acute affects**
  - *toxicity of hematopoietically active bone marrow*
- **Red bone marrow**
  - *hematopoietic stem cells (HSC)*
    - *Leukemia risk*
- **Trabecular endosteum**
  - *osteoprogenitor cells (OPC)*
    - *Bone cancer risk*
- **Both the skeletal endosteum and red bone marrow themselves serve as surrogate target tissues for underlying radiosensitive cell populations.**

Bone Tissue

- **Remodeling**
  - *Maintain constant Ca^{2+} and PO_4^{3-}*
  - *Mechanical stress*
- **Osteoporosis**
  - *Bone resorption > Bone formation*
  - *Most common bone disease in the United States*



Osteoporosis

- **Risk factors**
  - *gender, age, body size, ethnicity, family history*
  - *lifestyle*
- **Measured through bone mineral density (BMD)**
- **BMD (g/cm^2)**
  - *grams of calcium, other bone minerals*

low BMD

↓

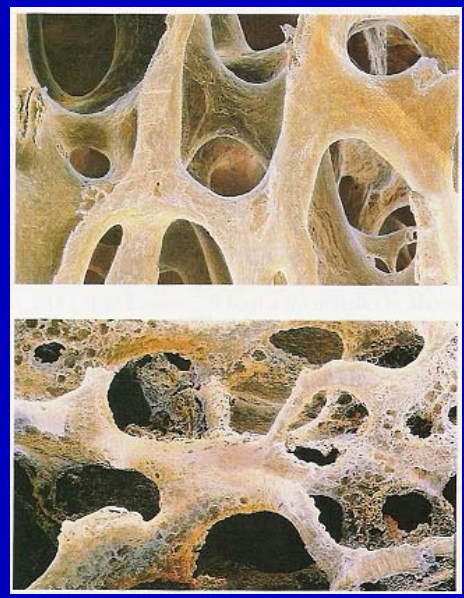
low mineral content

↓

less dense bones

↓

weaker bones



Bone Imaging Dosimetry Aims

- **Target tissue regions are used to determine absorbed fraction**
  - *Fraction of energy absorbed by the target tissue that was emitted by the source*
  - *Example: leukemia risk, target is red bone marrow*

$$S(r_T \leftarrow r_S) = \sum_i E_i Y_i \frac{\phi_i(r_T \leftarrow r_S)}{m_T}$$

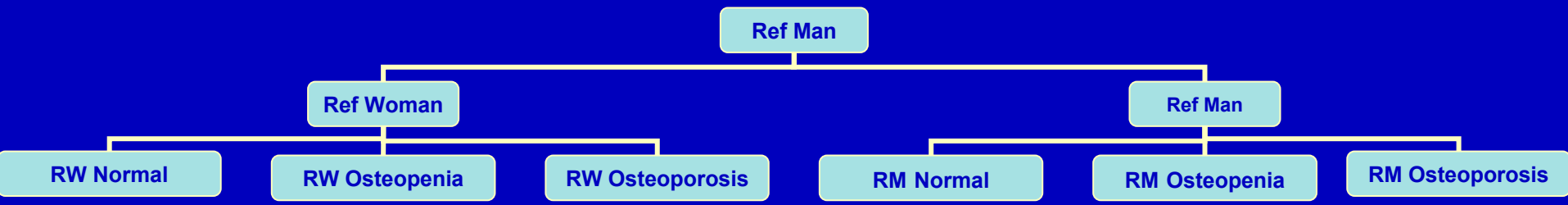
- **Optimize S value by making model specific to the patient**
  - *Account for patient skeletal size and percentage of active marrow*

- **MIRD absorbed dose estimate**

$$D(r_T \leftarrow r_S) = \tilde{A}_S \times S(r_T \leftarrow r_S)$$

Accurate Dose Estimates

- **Accurate and patient specific models are needed for the best possible dose estimates.**
  - *Properly model the tissue of interest*
    - *concentration and distribution of stem and progenitor cells within the hematopoietically active marrow*
  - *Reliable, scalable, reference models*
    - *Build a dataset of varying individuals*



Objectives

- **Develop a comprehensive reference female subject for gender specific skeletal dosimetry.**
  - *For use in all aspects of radiation protection and medical dosimetry*
    - *Scalable to a patient*
  - *Normal Bone health*
    - *No cancer, normal BMI*
  - *Provide adjustable mass and absorbed fraction data*
    - *Account for macrostructure (skeletal size) and microstructure (marrow volume fraction)*

$$\left(m_{TAM}\right)^{x}_{UF\text{-}RF} = \left(SV\right)^{x}_{UF\text{-}RF} \cdot \left(MVF\right)^{x}_{UF\text{-}RF} \cdot \left(CF\right)^{x}_{Variable} \cdot \rho_{TAM}$$

Skeletal Dosimetry Modeling

- **We cannot know the microstructure of the patient, nor can we guess the exact amount of energy deposited into a certain tissue beforehand.**
- **No female model to date**
  - *Osteoporetic state*
- **Current model uses multiple sources of data**
  - *Absorbed fractions* → University of Leeds chord distributions
  - *Marrow total mass and relative distribution* → Mechanic (1926)
  - *Reference marrow cellularities* → Custer (1974)
  - *Bone masses* → Trotter and Hixon (1974)
  - *Endosteal masses* → Leeds S/V ratios & ICRP thickness of 10 μm

Improved Transport

- **Paired Image Radiation Transport (PIRT)**
  - *Code developed through University of Florida Bone Imaging and Dosimetry (BID) group*
  - *Electron tracking through EGSnrc*
  - *voxel-based, three dimensional model*
- **Macrostructure**
  - *ex-vivo CT scan of an excised skeletal site*
  - *manually segmented trabecular spongiosa and cortical bone*
- **Microstructure**
  - *ex-vivo microCT scan of a cored section of spongiosa*
  - *30 μm high resolution*
  - *segmented using a novel image-gradient approach*
    - *marrow volume fraction (MVF) obtained*
    - *full range of marrow cellularity*

Paired Image Radiation Transport

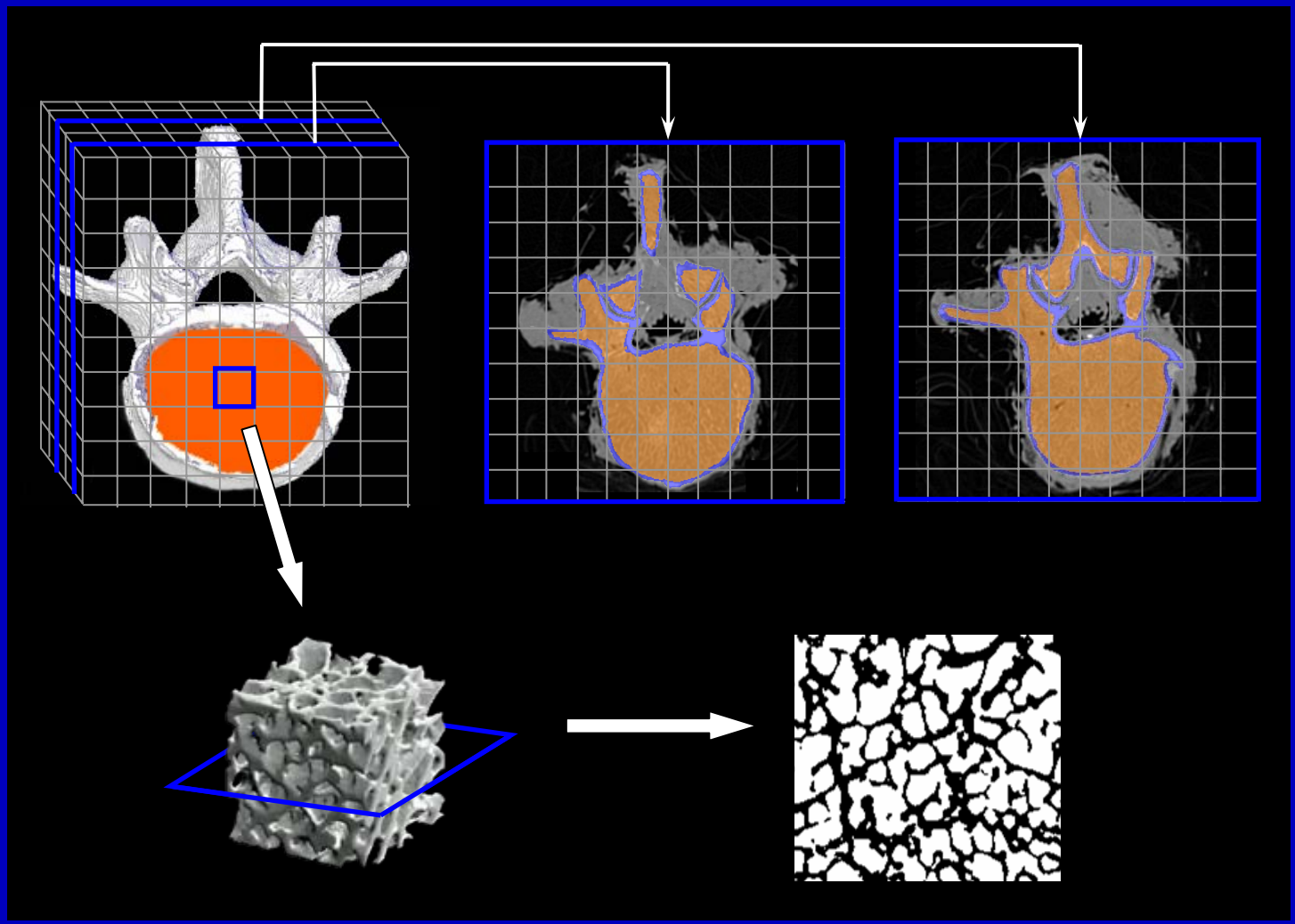
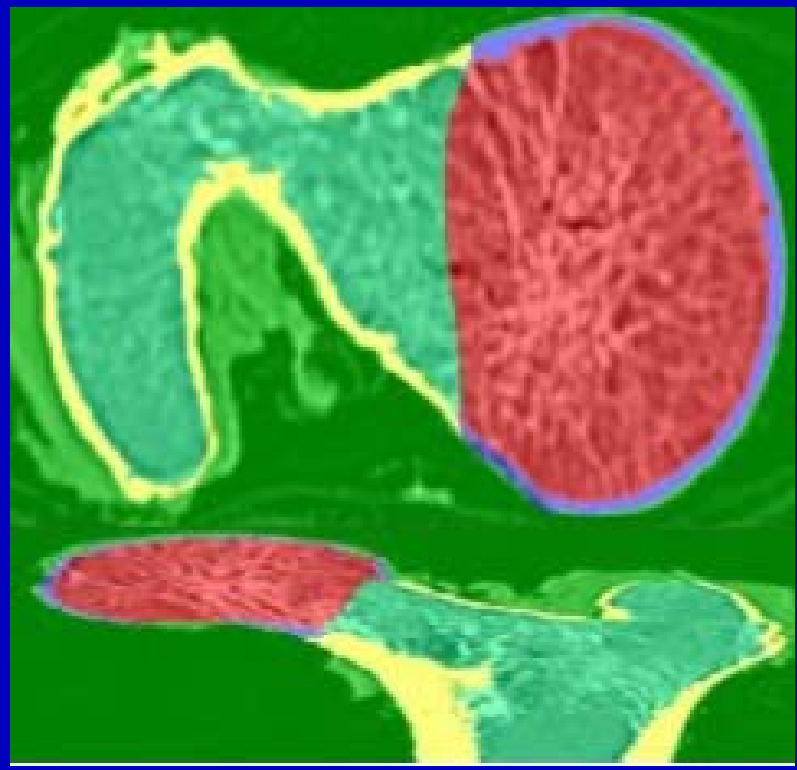


Image Based Skeletal Dosimetry

- **Cadaver selection**
  - *64 yr female, 22.51 kg $m^{-2,}$ no cancer*
- **Whole-body CT imaging**
- **Bone site harvesting**
  - *13 major sites of adult active bone marrow*
- **Ex-vivo CT imaging of each excised skeletal site**
  - *Volume measurements*
    - *Spongiosa → combined tissues of trabeculae, endosteum, active and inactive marrow*
- **Section skeletal sites – cubes of spongiosa**
- **Microimaging of spongiosa**
  - *30 micron resolution*
  - *Marrow Volume Fraction*

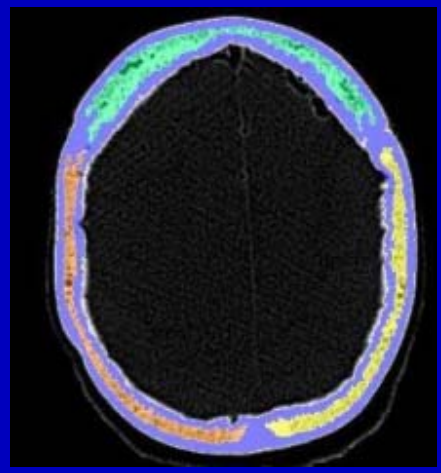
Ex-vivo Volume Estimates

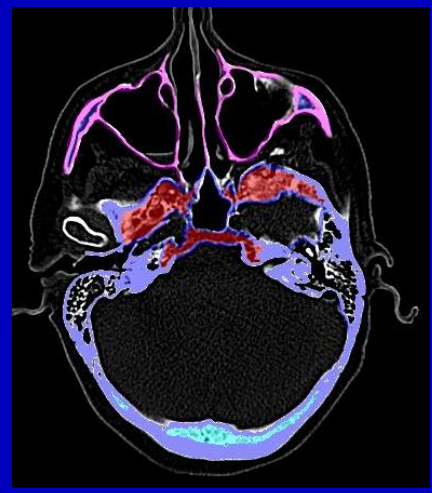
- **Femora**
  - *MVF varies*
  - *Head*
  - *Neck*



Detailed Volume Estimates

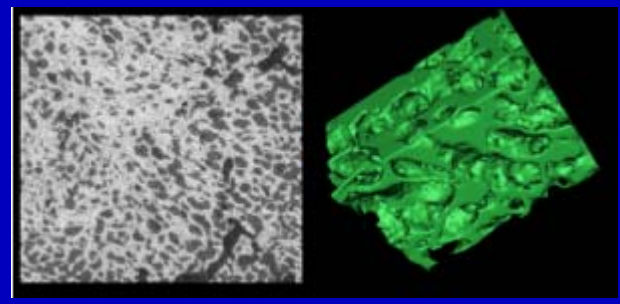
- **Cranium**
  - *MVF changes drastically between lobes*
    - *Left Parietal*
    - *Right Parietal*
    - *Occipital*
    - *Frontal*
    - *Others*
      - Ethmoid
      - Sigmoid
      - Temporal
    - *Facial*



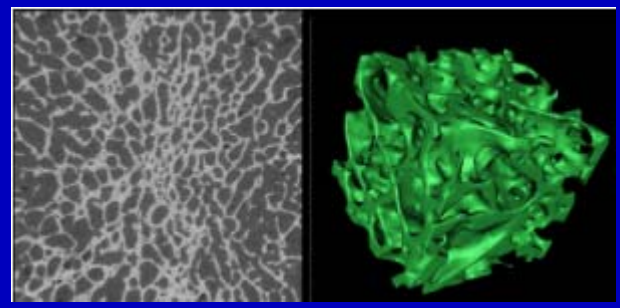


Large Microstructural Differences

- **Cranium, frontal**
  - *40% marrow*



- **Femora, head**
  - *71% marrow*



- **Due to weight loading**

Mass Within Trabecular Spongiosa Regions – Active Marrow Skeletal Sites

Skeletal Site (w /active marrow)	Trabecular Spongiosa Regions					Cortical Bone Regions	
	Spongiosa Volume (cm^3)	Marrow Volume Fraction	Endosteum Volume Fraction	Trabecular Bone Volume Fraction	Trabecular Bone Mass (g)	Cortical Volume (cm^3)	Cortical Bone Mass (g)
Os Coxae	407.65	0.87	0.06	0.13	98.70	212.99	408.93
Cervical Vert	31.67	0.78	0.10	0.22	13.19	4.88	9.36
Thoracic Vert	171.51	0.90	0.06	0.10	32.73	6.65	12.76
Lumbar Vert	151.47	0.91	0.05	0.09	27.48	13.60	26.11
Sacrum	83.25	0.96	0.02	0.04	5.63	40.84	78.41
Clavicles	25.94	0.96	0.02	0.04	2.02	9.99	19.17
Right	13.63	0.96	0.02	0.04	1.00	10.01	19.22
Left	12.32	0.96	0.02	0.04	1.02	9.96	19.13
Femora, proximal	205.94	0.81	0.08	0.19	75.72	33.33	63.99
Right	257.82	0.81	0.08	0.19	95.88	33.93	65.15
Left	152.06	0.81	0.08	0.19	55.21	32.69	62.77
Humeri, proximal	105.76	0.95	0.03	0.05	10.05	20.63	39.60
Right	*	*	*	*	*	*	*
Left	46.30	0.95	0.03	0.05	4.40	10.31	19.80
Scapulae	56.73	0.77	0.09	0.23	24.53	27.52	52.85
Right	28.48	0.87	0.06	0.13	6.95	28.27	54.28
Left	28.25	0.68	0.01	0.32	17.57	26.78	51.42
Sternum	30.59	0.99	0.01	0.01	0.73	16.23	31.16
Mandible	15.42	0.89	0.06	0.11	3.28	22.07	42.38
Ribs TOTAL	128.42	0.93	0.04	0.07	17.06	180.81	347.15
Cranium	132.62	0.37	0.14	0.63	160.50	262.41	503.82
Facial bones	1.86	0.89	0.06	0.11	0.40	24.90	47.80

Mass Within Trabecular Spongiosa Regions – Inactive Marrow Skeletal Sites

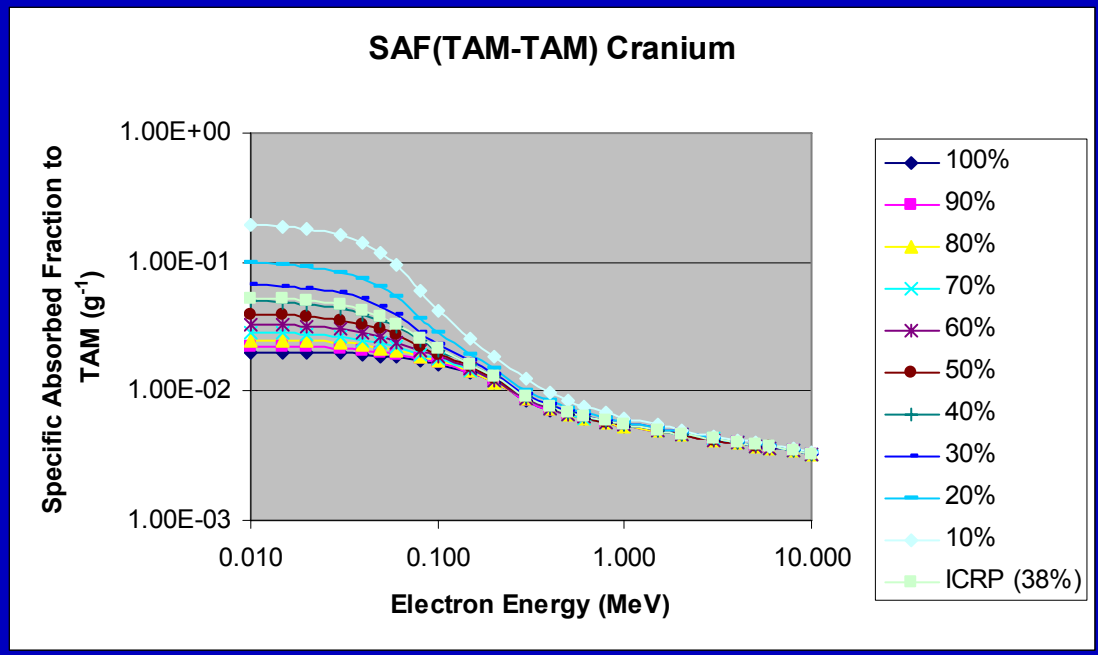
	Trabecular Spongiosa Regions					Cortical Bone Regions	
Skeletal Site w/o active marrow	**Spongiosa** Volume (cm^3)	**Marrow** Volume Fraction	**Endosteum** Volume Fraction	**Trabecular Bone** Volume Fraction	**Trabecular Bone** Mass (g)	**Cortical** Volume (cm^3)	**Cortical Bone** Mass (g)
Femora	340.93				75.83	254.28	488.22
medullary cavity	42.84	*	0.01	*	*	140.11	269.01
distal end	298.09	0.87	0.07	0.13	75.83	114.17	219.20
Fibula	45.15				7.15	57.76	110.91
proximal	14.76	0.87	0.07	0.13	3.76	8.00	15.37
medullary cavity	17.05	*	0.02	*	*	37.29	71.60
distal	13.34	0.87	0.07	0.13	3.39	12.47	23.94
Tibia	343.77				82.80	210.06	403.31
proximal	238.62	0.87	0.07	0.13	60.71	98.80	189.69
medullary cavity	18.31	*	0.01	*	*	56.37	108.22
distal	86.84	0.87	0.07	0.13	22.09	54.89	105.39
Humeri	53.56				2.55	36.59	70.25
medullary cavity	26.73	*	0.01	*	*	22.88	43.93
distal end	26.83	0.95	0.03	0.05	2.55	13.71	26.32
Ulna	19.30				1.28	38.27	73.48
proximal	10.46	0.95	0.03	0.05	0.99	12.66	24.32
medullary cavity	5.87	*	0.02	*	*	20.29	38.96
distal	2.97	0.95	0.03	0.05	0.28	5.31	10.20
Radius	27.27				2.21	44.17	84.81
proximal	8.42	0.95	0.03	0.05	0.80	9.29	17.84
medullary cavity	3.98	*	0.02	*	*	20.86	40.04
distal	14.87	0.95	0.03	0.05	1.41	14.03	26.93

Comparison to ICRP 70/89 – 35 Year Old Female

Subject Parameter	ICRP 70 35 y female Mass (g)	UF Reference Female Mass (g)	Difference %
height (cm)	163	160	
weight (kg)	60	61	
BMI kg/m^2	22.58	23.83	
Age	35	64	
Total Skeleton	7800	6587.96	18.40%
Bone	4000	3453.52	15.82%
Active Marrow	900	689.12	30.60%
Inactive marrow	1800	1345.33	33.80%
cartilage	900	900	
miscellaneous	200	200	

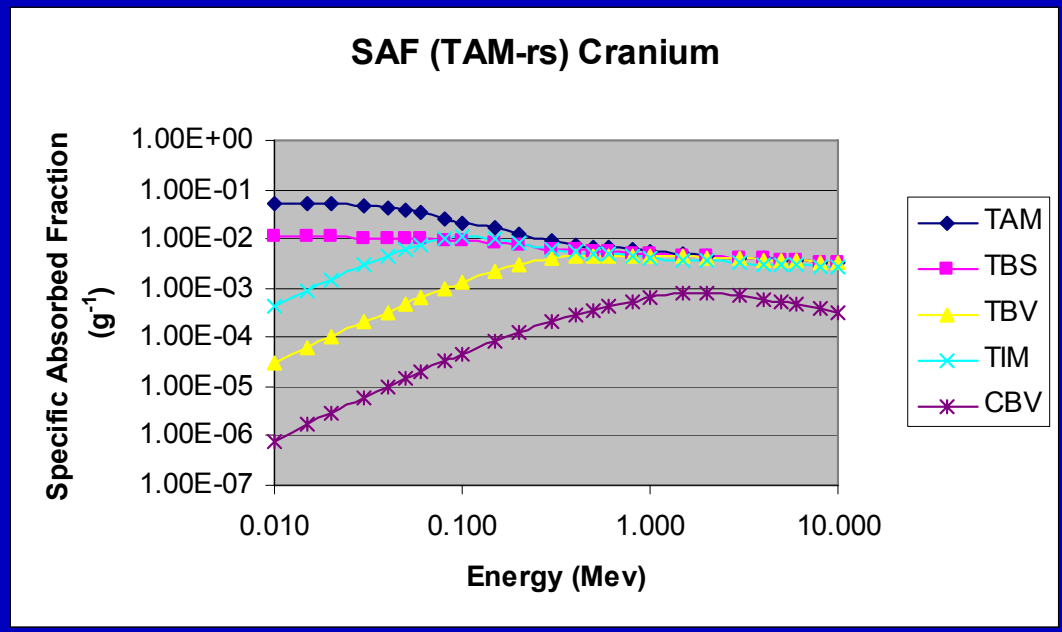
- **Assume same cartilage and miscellaneous mass**
  - *Miscellaneous: teeth, periosteum, blood vessels*
- **Total Skeletal**
  - *Sum of bone, active marrow, inactive marrow, cartilage, and miscellaneous*

SAF's for TAM←TAM



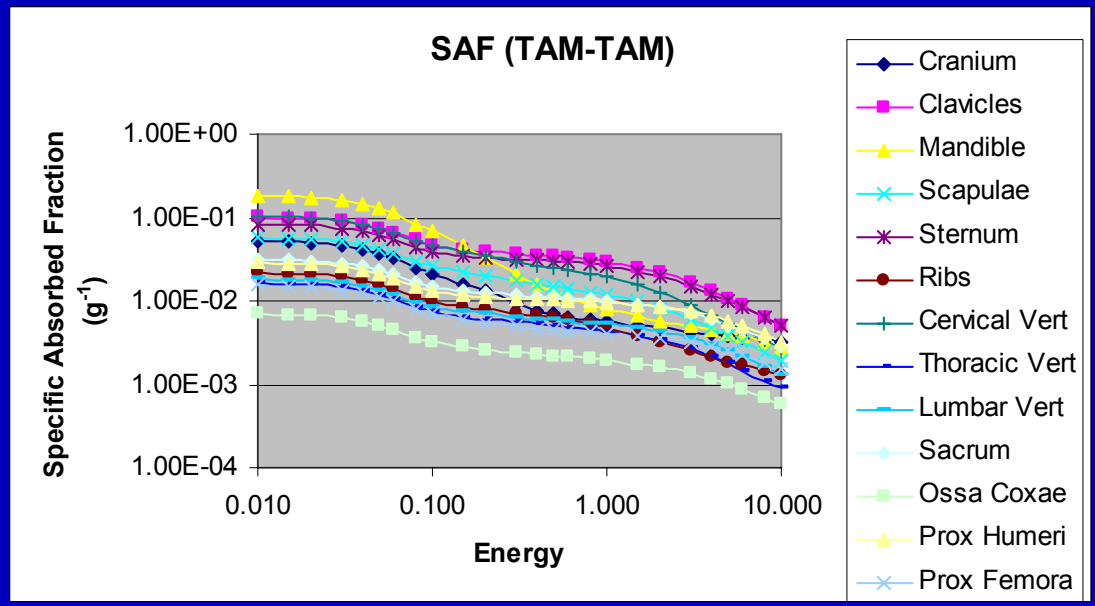
- **Specific Absorbed fraction calculated for TAM_{50}←TAM**
  - *Surrogate for HSC population*
  - *All skeletal sites containing active marrow*

SAF's for all Sources Irradiating the TAM



- Repeated for TAM_{50} as a target and all skeletal sites

SAF's Comparing all Skeletal Sites



- **Repeat for all source target combinations**

Future Work

- **Spatial distribution of blood vessels and hematopoietic stem and progenitor cells within the marrow cavities of human cancellous bone.**
  - *CD34+ and CD117+*
  - *Several skeletal sites*

- **Compare stem cell distributions for compromised marrow states**
  - *Pre and post-chemotherapy lymphoma patients*
  - *Better assess temporal status for radiation therapy*

This completes my presentation -
I would be happy to entertain questions at this time.