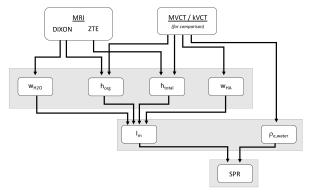
## Methodology for high-accuracy calculation of SPR using multimodal imaging

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**Introduction**: Proton therapy is becoming an increasingly popular cancer treatment modality due to the proton's physical advantage in that it deposits the majority of its energy at the distal end of its track where the tumor is located. Proton range in material is determined from the stopping power ratio (SPR), with errors in computing SPR from kVCT precluding the ability to utilize protons to their full potential. If achievable, using magnetic resonance imaging (MRI) to calculate SPR would provide numerous advantages. The goal of this work is to evaluate a multimodal imaging framework for determining SPR using synthetic tissues fabricated to emulate human biological tissues.

Materials and Methods: Synthetic tissues were created to mimic skin, muscle, adipose, and spongiosa bone. SPR was calculated using the Bethe Bloch equation from values of  $\rho_{e,water}$  (relative electron density) and  $I_m$  (mean ionization potential) determined for each tissue. The UC method of calculating  $I_m$  is outlined by Sudyhadhom<sup>1</sup> whereby  $I_m$  is computed at the voxel level (equation 1) using the Bragg Additivity rule of elemental composition assuming human biological tissue is composed of water ( $H_2O$ ), organic (org) material, and mineralized (hydroxyapatite; HA) material,

$$\ln I_{voxel} = \left(\sum_{i} \frac{w_{i}Z_{i}}{A_{i}} \ln I_{i}\right) / \left(\sum_{i} \frac{w_{i}Z_{i}}{A_{i}}\right) = \frac{\left(\frac{w_{H_{2}O}Z_{H_{2}O}}{A_{H_{2}O}} \ln(I_{H_{2}O})\right) + \left(\sum_{org} \frac{w_{org}Z_{org}}{A_{org}} \ln(I_{org})\right) + \left(\frac{w_{HA}Z_{HA}}{A_{HA}} \ln(I_{HA})\right)}{\sum_{total} \frac{w_{total}Z_{total}}{A_{total}}}$$
(1)



where for component i,  $w_i$  is the fraction by weight,  $Z_i$  atomic number, and  $A_i$  atomic mass. All variables above can be determined a priori, leaving  $w_{H2O}$ ,  $w_{org}$ ,  $w_{HA}$ , and h (hydrogen density by mass; used in calculating  $w_{org}$  and the denominator of equation 1) to be extracted from two MRI pulse sequences (DIXON fat-water separation and zero echo time, or ZTE) and CT as outlined in **figure 1**.

Figure 1: multimodal imaging framework for determining SPR using MRI and CT

**Results**:  $I_m$  and SPR results using the UC imaging method versus calculations from first principles are shown in **table 1**. The reported UC imaging method values use relative electron density from MVCT and physical density and  $w_{HA}$  from kVCT.

	I <sub>m</sub> (eV)		SPR	
	UC Imaging Method	Calculation	UC Imaging Method	Calculation
Skin	$77.3 \pm 1.4$	74.7	$1.05\pm0.01$	1.06
Muscle	$75.4 \pm 0.7$	74.1	$1.03\pm0.01$	1.04
Adipose	65.9 ± 1.9	68.5	$0.95 \pm 0.01$	0.95
Spongiosa	$68.7 \pm 1.0$	74.5	$1.04\pm0.01$	1.04

**Table 1**: I<sub>m</sub> and SPR values for UC Imaging Method versus ground truth calculations.

**Conclusion**: The UC method using multimodal imaging is able to achieve high accuracy in computing SPR with average percent errors of 1.1, 1.0, 0.3, and 0.7% for synthetic skin, muscle, adipose, and bone, respectively.

## References

Sudhyadhom A. Determination of mean ionization potential using magnetic resonance imaging for the reduction of proton beam range uncertainties: theory and application. *Phys Med Bio*. **62** (2017) 8521-35.