

The efficacy of biologically targeted radionuclide therapy (TRT) is dependent on the properties of the treatment strategy, the vector (carrier) molecule, the radionuclide products, and the target and normal tissue architecture. Both dose estimation and cellular response at the lower dose rates of TRT are more complex than typical external beam or high dose brachytherapies, for both targeted and normal tissues. Estimation of TRT response of target and normal tissues suffers from inaccurate macroscopic dose estimation, heterogeneous microscopic dose and dose rate dependence, and confounding factors including pretreatment patient status and treatment synergy with concurrent treatment regimens. Cellular response depends on cell survival, being influenced by apoptosis, damage repair, cell division delay, cell cycle redistribution, reoxygenation, regeneration and bystander effects. Tissue response can be described using the linear-quadratic model, including allowances for the effects of the above modifying factors. The demand for improved therapy (dose) response modeling, a prerequisite for improved therapy dose optimization, requires more extensive and detailed imaging. Effects that can be modeled using quantitative imaging are: 1) tissue changes over an extended therapy interval (e.g. SPECT/CT, dual energy CT); 2) macro and micro structure and activity distributions of targeted and normal tissues (e.g. SPECT/CT, autoradiography); and 3) macroscopic effects of cell response to therapy (e.g. PET/CT). To help accomplish this, increased efforts are being made to perform more frequent high-resolution imaging, along with potential correlation to biomarkers. Results point to characteristic non-uniform micro distributions that can be used to modify therapy-response estimates based on routine macro distribution measurements. Examples of the need for improved imaging include 1) evidence that imaging-based bone marrow doses correlate with outcome better than blood-based methods; 2) dose estimations from 3D (SPECT/CT) methods are significantly superior to 1D (planar) methods; 3) evidence that factors other than dose affect therapy outcomes, possibly with synergistic relationships with dose and dose rate.

#### Learning Objectives:

1. Understand the importance of quantitative imaging and reconstruction for therapy response modeling in TRT
2. Understand the importance of modeling biological effects in TRT in comparison to external beam therapy
3. Learn some approaches to therapy response modeling of TRT