Response to Therapy

Bone metastases response to therapy: MRI versus Nuclear Medicine

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Target Audience and scope: Radiologists, technologists and clinical support scientists. This talk will cover the challenges; evidence for use of different imaging technologies including current guidelines (RECIST1.1, MDA, PERCIST, PCWG2) and future directions.

Highlights: RECIST 1.1[1] based on CT size measurements is the most widely used criteria for response assessment in clinical trials but only bone metastases with a soft tissue component are considered evaluable. Although 99mTc-MDP bone scan has limited sensitivity the Prostate Cancer Clinical Trials Working Group 2[2] recommend it use due to its widespread availability and long track record. Although under investigation no PET/CT techniques have been robustly proven in the therapy response setting for metastatic bone disease. Data for whole body diffusion weighted MRI is promising but limited by availability and cost; evaluation of analysis methodology and response criteria are in evolution.

Challenges: Metastatic bone disease arguably remains the most challenging site for response assessment due to heterogeneity and widespread anatomical distribution.

Opportunities: The past few years have seen shifting enthusiasm for different imaging technologies. In the context of response assessment, cheap and widely available CT and 99mTc-MDP bone scintigraphy which image secondary effects of bone metastases on bone trabeculae lost favor due to lack of quantification and limited sensitivity and specificity to early changes. The combination of wide coverage, quantitative functional metabolic data and anatomy afforded by FDG PET/CT is highly attractive but not all metastases are FDG avid and in prostate cancer where the demand for response assessment of bone metastases is greatest, sclerotic metastases show less FDG uptake[3]. Fluoride PET/CT serves as a more sensitive and specific bone scan and there is rapidly emerging evidence for the use of choline PET/CT in the diagnosis of bone metastases in prostate cancer but there is no robust evidence in the therapy response setting and both FDG and choline uptake are reduced with hormone therapy[4]. Conventional MRI provides excellent contrast between normal and diseased bone marrow and makes RECIST size based assessments feasible [5] although this falls short where disease is diffuse. Whole body diffusion weighted MRI can be performed in reasonable time frames, can provide a quantitative assessment of disease and to some extent deals with tumor heterogeneity. Significant advances have been made in sequence development and understanding response assessment with this tool but as with PET/CT the numerous areas of potential variability for data acquisition and interpretation have not been resolved. These factors combined with significant costs have drawn some centers to refocus efforts towards simpler and more cost effective techniques. For example response shown by 99mTc-MDP bone scan index which quantifies disease burden on MDP bone scintigraphy has recently been shown to be a strong indicator of prognosis and correlates with overall survival [6,7]. Heterogenity in metastatic bone disease means that a “one size fits all” methodology is destined to be flawed but some may consider this the most pragmatic approach. Response criteria tailored to tumor types will increase accuracy but also complexity and these directions must be agreed by international concensus.

References: 1.Eisenhauer ET et al EJC 2009; 45:228-247; 2.Scher HI et al JCO 2008;1148-59; 3.Fogelman I et al Sem Nuc Med 2005; 35:135-42; 4.Langsteger W et al Sem Nuc Med 2006;36:73-92; 5.Tombal et al Prostate 2005; 65:178-87; 6.Dennis ER JCO 2012;30:519-34; 7.Mitsui Y BJU 2012; epub ahead of print.