Figure 1. Heterogeneous distribution of trastuzumab.

Trastuzumab was administered to Her2+ xenograft-bearing mice. Multiplex immunohistochemistry shows vasculature (CD31, dark blue), perfusion dye (carboycanine, cyan) and trastuzumab (red) after a 26h exposure. By 26h most vessels have at least some trastuzumab binding of perivascular cells, but independent of vascular density (high, left; low, right) there remain some vessels with less trastuzumab. This intra-vessel heterogeneity in trastuzumab distribution results in some tissue remaining unexposed to systemically administered trastuzumab. Scale bars 200µm. [Baker et *al.*, 2008. Clinical Cancer Research 14(7); p2171].

20 mg/kg trastuzumab, 26 h



Figure 2. Hyperbranched polyglycerol (HPG) as multi-modal imaging agent.

Images of (A) HPG fluorescence in a tumour cryosection and (B) HPG concentration from calibrated changes in RI relaxation rate of the same slice and orientation. Corresponding TI-weighted RARE MR images are shown (C) prior to and (D) 40min post-injection of HPG.. [Saatchi, et al., 2012. Bioconugate Chemistry 372(23); p372].



Figure 3. Correlating MR imaging with histological analysis.

Excellent correlations between MR and histological images are obtained using implanted fiducial markers constructed of polyethylene tubing filled with saline and paraffin. This marker, detectable using both modalities, enables re-imaging of the same planes in different modalities and on multiple days. Markers (left) shown in MR images (middle) and in histological image of vascular staining (right).



Figure 4. Experiment workflow.

A typical experiment workflow involves MR imaging of Her2+ xenografts (A) followed by histological processing and multiplexed immunostaining (B) such that images from both modalities may be overlayed for contextual analysis (C).



Analysis

Tumour maps (i) are co-registered and quantitatively compared with DCE-MRI parameter maps (ii) to get correlative data (iii).



Figure 5. Correlating MRI and histological images for quantitative analysis.

MRI-derived biomarkers such as IAUC are displayed as parameter maps (top) and are compared to histological images of perfusion that are downsampled or at full resolution (middle), enabling comparison of detailed microenvironmental features at high resolution (bottom) to those of MRI. These comparisons are verified quantitatively in a correlative chart. [Bains, Baker et al., 2009. Int J Rad Oncol Phys 74(3); p957].

