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Angiogenesis and Metabolism in cancer; Molecular and Physiological characterization by means of MRI/MRS.

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We have investigated tumor growth, progression and metastasis, using molecular and cellular methodologies, as well as non-invasive imaging and spectroscopic techniques based on magnetic resonance. The studies were conducted in human breast, prostate and lung cancer cell cultures and tumors developed in animal models. In addition, clinical investigations of breast and lung cancer patients were performed by means of MRI and CT, respectively.

The research focused on the following topics:

1. Estrogen regulation of breast cancer angiogenesis
2. Vascular physiology of benign and malignant breast lesions and of metastases to lymph nodes, bones and lungs.
3. Choline transport and metabolism in the course of malignant transformation of epithelial cells.
4. Mechanism(s) of glucose transport and glycolysis in breast cancer and their modulation by induced differentiation..
5. Quantifying response of breast cancer patients to chemotherapy by means of dynamic contrast enhanced MRI (Figure 1).

Specific efforts were directed to develop and improve non-invasive magnetic resonance imaging (MRI) and spectroscopic (MRS) methods that quantified tissue physiologic and metabolic processes. With these methods we were able to monitor dynamic processes at steady state and during changing conditions. Specifically, we have characterized flow and permeability limited perfusion, water and contrast agent diffusion, convection and the disparity in perfusion due to interstitial fluid pressure (Figure 2). We also developed the means to monitor glucose transport and glycolysis *in vivo* and designed MRI sensitive molecular probes that can bind specifically to the estrogen receptor and thereby map its distribution.

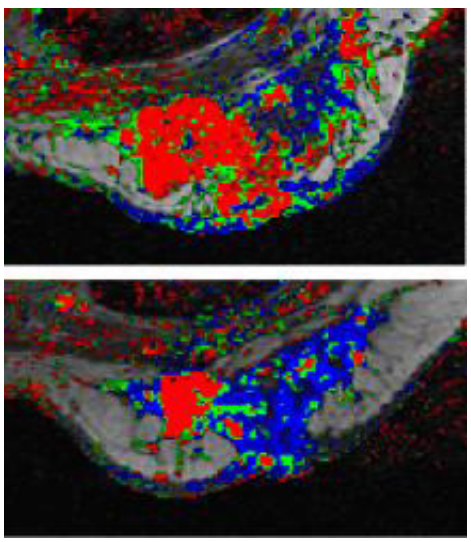

Fig. 1 *3TP images of breast cancer before (top) and after 4 courses of chemotherapy (bottom) indicating partial response to therapy. The red regions in the breast represent cancerous tissue. After therapy the blue regions represent reparative, fibrous tissue that responded to the treatment.*

Selected Publications

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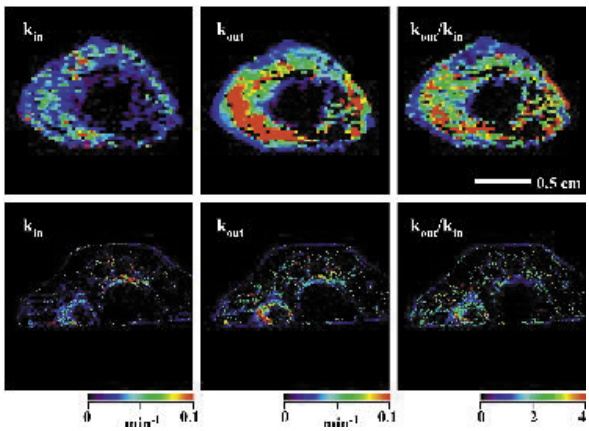

Fig.2 *Parametric image of the disparity in the transcapillary transfer constants (kin /kout) of MDA-MB- 231 breast tumor inoculated in the mammary of a SCID mouse. The lower panel demonstrates the parameters in an axial slice through the mouse lower abdomen. The tumor on the left has higher transcapillary transfer constants than other parts of the body. The upper panel demonstrates the spatial distribution of the transcapillary transfer constants in the tumor tissue.*

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