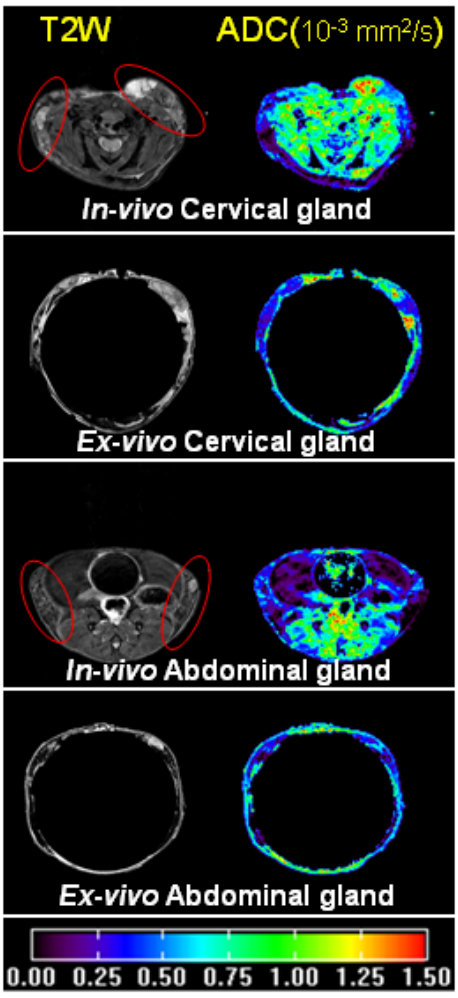
A novel technique for correlating between in vivo and ex vivo whole body mammary glands: Comparison of apparent coefficient values

Xiaobing Fan[1], Kay Macleod[1], Suzanne Conzen[1], Erica Markiewicz[1], Marta Zamora[1], James Vosicky[1], Devkumar Mustafi[1], and Gregory Karczmar[1]
[1]*University of Chicago, Chicago, IL, United States*

Target audience: This study will benefit the people who are interested in the mouse model of breast cancer, and correlation between *in-vivo* and *ex-vivo* mammary glands.

Introduction: Transgenic female mouse models are often used in pre-clinical research to understand progression of breast cancer. Correlations between *in vivo* and *ex vivo* MRI, as well as with histology, are often performed to confirm the type and stage of cancer [1-3]. Previous studies in transgenic mouse models demonstrated that not all ductal carcinoma *in situ* (DCIS) lesions may progress into invasive cancers, and tumorigenesis is accelerated in upper glands, i.e., at cervical and thoracic glands for SV30Tag mice [2]. Diffusion weighted imaging (DWI) has been increasingly used to detect breast cancer. However, correlation of whole body mouse mammary glands between *in vivo* and *ex vivo* DWI MRI has not been done and remains a challenge. Here, we report a novel approach to imaging whole body mouse mammary gland to correlate *in vivo* and *ex vivo* MRI and evaluate the ADC values. The polyoma middle T oncoprotein (PyMT) mice, which have been proved to be an excellent model to understand the biology of tumor progression in humans, are used in this study.

Methods: Four adult PyMT mice were imaged at 9.4T; whole-body scanning was used to study all of the mammary glands. For *in vivo* experiments, multi-slice RARE (Rapid Acquisition with Relaxation Enhancement) spin echo T2-weighted images with fat suppression were acquired to identify abnormal regions (TR/TE_{effect} = 4000/26 ms, FOV = 30 mm, matrix size = 256^2, slice thickness = 0.5 mm, NEX = 2, RARE factor = 4) for upper and lower mammary glands separately. Then DWI was performed (TR/TE = 4000/26 ms, b-value = 0, 1000, and 3000 s/mm^2, FOV = 30 mm, matrix size = 128^2, slice thickness = 1.0 mm, NEX = 1) for nine slices selected based on the T2W images. To facilitate correlation of *in vivo* and *ex vivo* images, two standards (1 mm diameter tube filled with water) were placed at 5 mm from the 1st nipple from top and the last nipple from the bottom for both *in vivo* and *ex vivo* scans. For *ex vivo* experiments, the skin and glands were taken by carefully excising the skin from the mouse. A midline incision along the ventral abdomen was made from the tail to the head; and then the skin, glands, and tumors were gently peeled from the body muscle so that the hide remained intact. Once formalin fixed, the tissue was placed around a fomblin filled tube and sutured together back along the midline to resemble the round shape of a mouse. This skin and tube were then placed in a larger tube, filled with fomblin, and sealed before being placed into the 35 mm diameter quad coil. The same pulse sequences used for *in vivo* experiments were also used for *ex vivo* experiments.



Results: The figure shows fat suppression T2-weighted images (left panel) and corresponding ADC maps (right panel) for both *in vivo* and *ex vivo* set-ups at the cervical and abdominal glands. The abnormal mammary gland regions are circled in red on the T2-weighted images. As we can see, most abnormal regions had ADC values between ~0.25 to ~0.75×10^{-3} mm^2/s in both *in vivo* and *ex vivo* experiments, which are close to reported values from other clinical studies. There are also small regions with ADC values > 1.0×10^{-3} mm^2/s. Due to a lack of landmarks and the potential for the skin to be slightly stretched causing deformation in the *ex vivo* images, it is hard to visually directly compare *in vivo* and *ex vivo* images. Nevertheless, small, distinct features, such as lymph nodes and small tumors, correlated well in full size images between *in vivo* and *ex vivo* images.

Discussion: To our knowledge, this is the first report of correlation between *in vivo* and *ex vivo* MRI of whole body mouse mammary glands. With this technique, features found on *in vivo* slices can be found on *ex vivo* slices and then accurately identified in fixed tissue, and correlated with histopathology. The ADC values calculated from both *in vivo* and *ex vivo* DWI were reasonable. The motion-free *ex vivo* ADC maps may assist us in finding values that characterize DCIS, invasive tumor and lymph node *in vivo*. More quantitative analysis and correlation with histopathology are under way to evaluate the ADC for detection and diagnosis mammary cancer, and to understand cancer progression.

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[1] Jansen et al. Phys Med Biol. 2008; 53:5481-93. [2] Jansen et al. Breast Cancer Res. 2009; 11:R65. [3] Jansen et al. NMR Biomed. 2011; 24:880-7.