Correlation between *in vivo* and *ex vivo* MRI of mouse mammary glands with regards to apparent diffusion coefficient and T2 values

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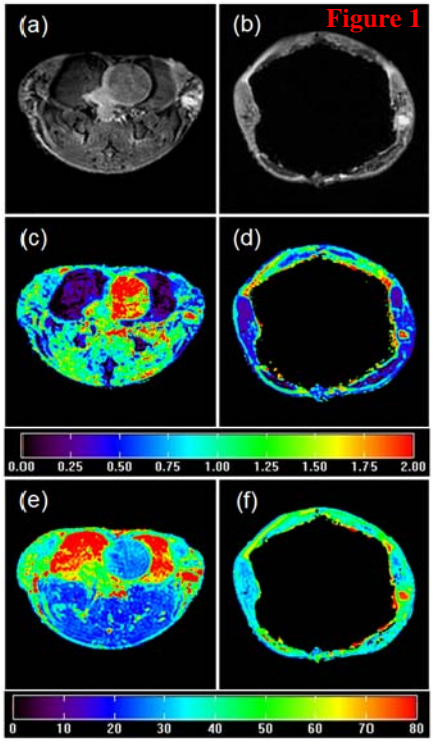
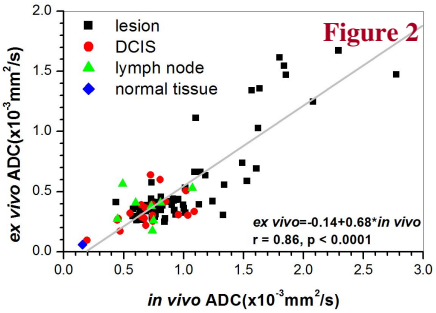
Target audience: This study will be of interest to investigators who study mouse models of breast cancer, use *ex vivo* MRI to evaluate water diffusion and T2, and/or use *ex vivo* MRI to guide evaluation of surgical specimens.

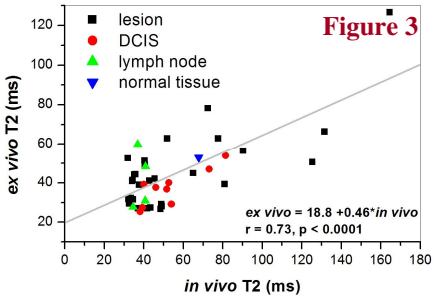
Introduction: There is increasing interest in *ex vivo* imaging of tissue and organs for studying micro-anatomy. In addition, *ex vivo* imaging could help surgeons and pathologists to identify tumor margins in surgical specimens. Transgenic female mouse models are often used in pre-clinical research to understand progression of breast cancer. Correlations between *in vivo* and *ex vivo* MRI, as well as histology, are often performed to confirm the type and stage of cancer.[(1-3)] Here we investigated the correlations between *in vivo* and *ex vivo* images of ADC and T2 in murine mammary gland tumors. Diffusion and T2 are important sources of contrast in breast imaging that do not require contrast media injection. Therefore, they are particularly relevant for *ex vivo* imaging.

Methods: Adult PyMT mice (n = 7) were imaged at 9.4T with a 35 mm quad coil. For *in vivo* experiments, multi-slice RARE (Rapid Acquisition with Relaxation Enhancement) spin echo T2-weighted (T2W) images with fat suppression were acquired to identify abnormal regions (TR/TE_{effect} = 4000/26 ms, FOV = 25.6 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, 500, 1000, and 1500 s/mm^2, FOV = 32 mm, matrix size = 128^2, slice thickness = 1.0 mm, NEX = 1) for nine slices selected based on the T2W images. For *ex vivo* experiments, a midline incision along the back spine 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. The tissue was fixed in formalin, washed in phosphate buffered saline and then placed around a mouse-sized sponge and sutured back together along the midline to mimic the geometry of the gland when attached to the mouse. This skin was then placed in a larger tube filled with fomblin. The same pulse sequences used for *in vivo* experiments were repeated for *ex vivo* experiments. For ADC and T2 measurements, the k-space data was zero-padded prior before Fourier transform so that the final image size was four times larger than the original image. This greatly facilitated tracing regions-of-interest (ROIs). Pixel-by-pixel analysis was performed to obtain ADC maps and T2 maps. ROIs were manually traced on T2W images to define features that could be identified on both *in vivo* and *ex vivo* T2W images. A total of 14 – 15 pairs of similar size ROIs were traced for each mouse.



Results: Figure 1 shows that similar features are well-matched on *in vivo* (left panel) and *ex vivo* (right panel) T2W images (a, b), corresponding ADC maps (×10^{-3} mm^2/s) (c, d), and T2 maps (ms) (e, f). Figure 2 shows the scatter plot (n = 7 mice) of *in vivo* versus *ex vivo* ADC's, and demonstrates a strong positive correlation (r = 0.86, p < 0.0001). Finally, Figure 3 shows the scatter plot (n = 3 mice) of *in vivo* versus *ex vivo* T2's, and demonstrates a strong positive correlation (r = 0.73, p < 0.0001). The paired t-test showed that *in vivo* ADC values were significant larger (p < 0.004) than *ex vivo* values; and the *in vivo* T2 values were significant higher (p < 0.02) than *ex vivo* values, except in lymph nodes.





Discussion: These results demonstrated strong positive correlations between ADC and T2 values in *in vivo* and *ex vivo* mouse mammary glands. The *ex vivo* ADC's and T2's measured at 9.4 Tesla are about 0.65 and 0.45 times the *in vivo* values, respectively. Although the absolute values differ, the strong correlation between *in vivo* and *ex vivo* measurements suggests that the same processes that determine ADC and T2 contrast *in vivo* also are relevant for *ex vivo* images. Therefore, the motion-free *ex vivo* ADC and T2 maps may be useful for optimizing methods, and finding ADC and T2 values that characterize *in situ* cancers, invasive tumors and lymph nodes *in vivo*.

Conclusion: The strong similarity between *in vivo* and *ex vivo* images suggests that *ex vivo* imaging could serve as an aid to pathologists to improve the sensitivity, specificity, and speed with which tissue can be evaluated.

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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.