MR Microscopy - Ultra-High Resolution 7T MRI in Pathologic Analysis of Resected Breast and Lymph Tissue

Brittany Dashevsky[1], Krishna Juluru[1,2], Timothy D'Alfonso[1], Elizabeth Sutton[2], Eric Aronowitz[1], Ashley E. Giambrone[1], and Doug Ballon[1]
[1]*Weill Cornell Medical College, New York, NY, United States,* [2]*Memorial Sloan Kettering Cancer Center, New York, NY, United States*

Target Audience: Clinicians and scientists interested in breast MRI and ultra-high resolution MR microscopy.

Purpose: The in-plane spatial resolution of standard diagnostic breast MRI is 1 mm, which is sensitive (94%), but lacks specificity (26%) in the detection of breast cancer (1). In addition, the current time from percutaneous biopsy surgical resection of suspicious breast pathology to diagnosis is limited by histopathologic processing which takes at least 12 hours. Ultra-high resolution images obtained from 7 Tesla MR microscopy may be a tool that can expedite the pathological diagnosis, but there are few studies to date that evaluate this tool's performance in breast and lymph tissue (2). The purpose of this study was to 1) develop a technique for obtaining ultra-high resolution 7T MR images of common breast and axillary lymphatic pathology, and 2) to evaluate this technique by performing a reader study comparing 7T MR microscopy to traditional H&E stained pathology specimens.

Methods: We performed a HIPAA compliant IRB approved prospective study on 10 subjects. Resected breast and axillary lymphatic tissues were obtained from surgical biopsy or elective reduction mammoplasty. Fresh specimens were sliced into 3-4 mm sections by a pathologist and a single section was placed into a standard pathology cassette and immersed in 0.9% saline with 1% Gd-DTPA. MR images were acquired on a 7T, 30-cm bore Bruker Biospec MRI system utilizing an in-house, custom built solenoidal transmit/receive coil. Images were obtained using a gradient echo, T1-weighted sequence, with and without fat suppression at an in-plane spatial resolution of 60 x 60 µm and 94 µm slice thickness in 57 minutes. The remainder of the tissue was fixed in formalin and underwent routine processing and light-microscopy evaluation from 5.0 µm thick H&E stained sections. 7T MR and light microscopy images were then reviewed by 14 blinded breast pathologists, with no training in MRI, who completed a survey where they selected the diagnosis for each specimen. Rates of correct diagnosis, correct disease process (benign vs. malignant), and correct tissue characterization (breast vs. lymphatic) were calculated and compared with light microscopy responses, using a two-sample proportion test.

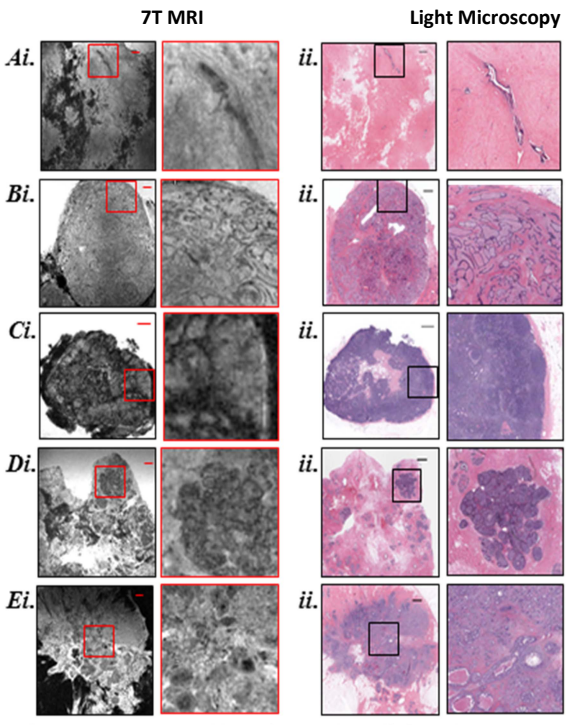

Figure 1. 7R MR *(i)* and corresponding light microscopy H&E stained images *(ii)* of resected specimens. Scale bar at top right is 1.25 mm. The areas within the boxes are magnified on the right. Normal breast parenchyma (A), fibroadenoma (B), benign lymph node (C), DCIS (D), and IDIC and DCIS (E).

Results: 7T MR images were obtained from 10 specimens yielding normal breast parenchyma (n=3), fibroadenoma (n=2), ductal carcinoma in situ (DCIS) (n=1), invasive ductal carcinoma (IDC) and DCIS (n=1), invasive lobular carcinoma (ILC) (n=1), in addition to benign (n=1) and malignant (n=1) axillary lymph nodes, within 1.5 hours of surgical excision. Representative images are shown in **Figure 1**. In all cases we achieved excellent spatial correlation between MRI and light microscopy using our apparatus. 7T MRI revealed fine details of the terminal duct lobular unit (A), as well as the distinct architecture of fibroadenomas (B) and lymph nodes (C), where the lymph node capsule was clearly delineated. Malignant pathology was identified by a loss of normal ductal/lobular architecture, for example with expansion of ducts for DCIS (D), or the presence of an enhancing mass with spiculations for IDC (E). In this untrained reader study, breast pathologists selected the correct diagnosis for 36% of cases; the correct disease process for 56% of cases; and the correct tissue type for 86% of cases, compared to 92%, 99% and 99% respectively, utilizing light microscopy images of H&E stained specimens. The results were significantly different for 7T MR versus light microscopy in determining the correct diagnosis ($p = 0.01$) and disease process ($p = 0.02$). There was no significant different between the two modalities in selecting tissue type ($p = 0.29$). However, pathologists correctly selected a malignant versus benign disease, with no significant difference between MR and light microscopy for the following specimens: benign lymph node, DCIS, IDC and DCIS, and ILC. Table 1 illustrates pathologists' responses to the MR images for each pathologic diagnosis.

Discussion: Our preliminary data demonstrates the ability to image breast and axillary lymphatic pathology with ultra-high resolution 7T MR images within 1.5 hours of specimen excision, with a spatial resolution of 60 x 60 x 90 µm yielding several characteristic pathologic imaging features which are visible to pathologists with no prior training in MRI. A larger scale training study is planned with the goal of enabling future MR microscopic diagnosis within hours.

Pathologic Diagnosis (Gold Standard)

Diagnosis based on 7T MR Images	ILC*‡	IDC and DCIS*‡	DCIS*‡	Malignant LN‡	Benign LN*	Fibroadenoma	Normal Breast Parenchyma‡
ILC	21%	7%				4%	17%
IDC	36%	7%	7%				45%
IDC and DCIS	21%	14%	14%	7%	7%		2%
DCIS	7%	57%	64%		14%	4%	12%
Malignant LN				36%	14%	29%	
Benign LN				57%	36%	4%	
Fibroadenoma					29%	57%	
Normal Breast Parenchyma	14%	14%	14%			4%	24%

When comparing the diagnosis utilizing 7T MRI vs light microscopy:
* p>0.05 for benign vs. malignant
‡ p>0.05 for breast vs. lymph tissue

Table 1. Survey results of the diagnosis utilizing representative 7T MR images of each specimen, against the pathologic gold standard. The correct diagnosis is highlighted in gray. 14 untrained, blinded pathologists completed the survey.

Conclusion: The pilot study suggests that pathologic diagnosis is possible using MR microscopy, and that this technique may play a role in the future management of breast cancer.

References: 1. Berg WA, Gutierrez L, NessAiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology. 2004; 233(3):830-49.
2. Menezes GL, Knuttel FM, Stehouwer BL, Pijnappel RM, van den Bosch MA. Magnetic resonance imaging in breast cancer: A literature review and future perspectives. World journal of clinical oncology. 2014;5(2):61-70.