Correlating MRI to the Gold Standard of Pathology in Invasive Breast Cancer

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INTRODUCTION

Despite the widespread use of MRI in the diagnosis and follow up of breast cancer following chemotherapy, there have been very few studies that compare MRI metrics to the gold standard of histology, especially in the clinical setting. Difficulties arise because of the large discrepancy in spatial resolution between histological sections (tens of microns) and imaging slices (thousands of microns). We are developing a methodology to register histology volumes obtained from mastectomy specimens to imaging volumes that would allow for quantitative comparison on a near voxel by voxel basis. The long term goal is to correlate relevant histological findings with dynamic contrast enhanced MRI (and other) parameters.

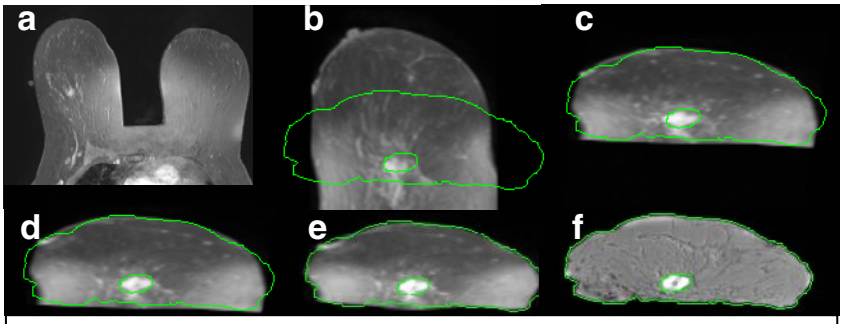

Figure 1. Panel a is the original *in vivo* MR image, f is the original *ex vivo* MR image, and b is the selected ROI with the green target (panel f) overlay; panel c displays the registration of b to via the RPM algorithm; panels d and e show the registration of the *in vivo* image to the *ex vivo* image with ABA applied on the tumor area and the whole volume, respectively.

METHODS AND RESULTS

Patients with clinical stage II/III carcinoma who would be undergoing mastectomy as a component of clinical care were enrolled as part of an IRB-approved study (1).

There are three components to the registration: 1) registration of *in vivo* MR images to *ex vivo* MR images of mastectomy specimens; and 2) registration of the *ex vivo* MR images to histological images. Once these two transformations are computed, they can be composed to register the in vivo and histological images (step 3).

Registration of pre- and pos-resection images There is a substantial difference in shape between the pre- and post-resection image volumes because the pre-resection images are acquired with the patient laying prone while the post-resection images are acquired with the specimen placed on a flat surface (panels a and f, respectively, **Figure 1**). To facilitate registration, the tumor is first segmented both in the pre- and the post-resection images. Then a rigid body transformation that realigns these two regions is computed via a standard Mutual Information-based algorithm (2). This transformation is then applied to the entire breast. The points from the tumor and breast boundaries in the two images are then extracted automatically and the Robust Point Matching algorithm (3) is applied to register these points. Results obtained after this non-rigid registration step are shown in Fig. 1c. The next step registers the entire volume using our adaptive bases algorithm (ABA) (4); first we register the area close to the tumor (where we use a stiff transformation as the tumor is typically stiffer than surrounding tissue), then freeze the transformation over this region and register the rest of the breast with a more elastic transformation. Fig. 1e shows the final result with this approach.

Registration of post-resection and histological images First, the MR slice that corresponds best to the histological image is extracted from the MR volume manually. Next, a point-based rigid body registration algorithm is used to register the two images. Homologous points required by this algorithm are selected manually in the histological and the MR images. To compensate for the shrinkage that occurs when the specimen is fixed, the rigid body registration is followed by a non-rigid registration step. This is done with the ABA algorithm using a high stiffness constraint to produce a smooth and regular transformation. Results we have obtained with this approach are shown in **Figure 2**; the histology image (purple) is a formalin fixed, paraffin embedded block stained with Hematoxylin and Eosion (H&E) and used to make a pathologic map of the tumor. Panels a, b, and c show the H&E and MR images (gray level) before registration, after rigid body registration, and after non-rigid registration, respectively. Panel d is a zoomed version of panel b and panel e is a zoomed version of panel c to show the overlap of the H&E stain on the MR image.

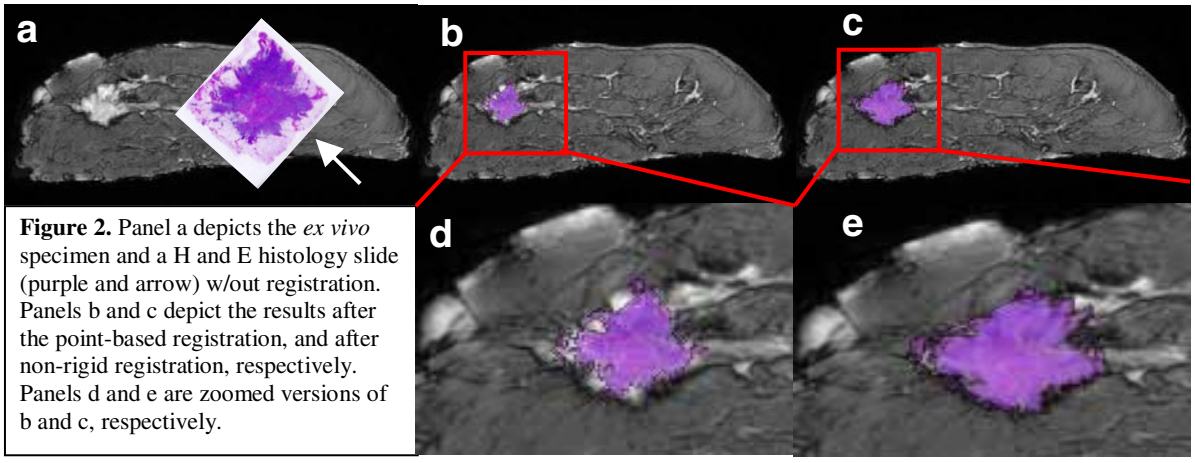

Figure 2. Panel a depicts the *ex vivo* specimen and a H and E histology slide (purple and arrow) w/out registration. Panels b and c depict the results after the point-based registration, and after non-rigid registration, respectively. Panels d and e are zoomed versions of b and c, respectively.

CONCLUSION

These results show that it is possible to perform each component of the cross-modality registration process. We are currently synthesizing these two steps so that the H and E histology stain can be registered to dynamic contrast enhanced MRI (and other) parametric maps.

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