

# Evaluation of Spatial Changes of Fibroglandular Tissue in the Breast between Two Scans Using Non-rigid Registration

## Method

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### Background and purpose:

The American Cancer Society recommends that women with lifetime risk greater than 20% should receive annual breast MRI for screening. Since these high-risk women will receive MRI every year, it would be very helpful to develop a co-registration method so that the current MRI can be compared with the MRI done the year before. This is similar to reading of mammograms by comparing to prior mammograms on the side, so the changes can be easily picked up for determining whether they are significant. This tool will also help radiologist decide whether a region needs to be followed closely, or further, whether it is suspicious of malignancy and warrants a biopsy. This task may be accomplished by registration between two MRI's taken at different times. The challenge is the positioning differences between two scans, particularly given the highly deformable nature of the soft breast tissues. In this work we developed a method using rigid and non-rigid Demons registration algorithm for breast co-registration done in 2 scans. The algorithm was applied to patients receiving neoadjuvant chemotherapy to evaluate the spatial shrinkage pattern of density after chemotherapy, as well as in normal volunteers for evaluating the menstrual-cycle related changes in density.

### Methods:

Six patients (age 31-64) were selected from a cohort of patients receiving neoadjuvant chemotherapy, and the MRI of the normal breast in the pre-treatment baseline and post-chemo follow-up studies were compared. 15 healthy volunteers (age 23-61) received two MRI's with one week apart are used as controls. These volunteers may show menstrual cycle related changes, but these are expected to be minimal compared to chemotherapy induced breast density atrophy. The fibroglandular tissues were segmented [1], by using an improved bias field correction algorithm based on combined N3 [2] and fuzzy C-means (FCM). The segmented density in B/L and F/U were rigidly aligned first, and then Demon's algorithm [3-4] was applied to deform the density in B/L to match the density in F/U. Since Demon's algorithm can match topological features during coregistration [3], the collapse of multiple voxels at B/L into one voxel at F/U indicates shrinkage. A higher number of overlapping voxels indicate a greater shrinkage in that area. Expansion is analyzed based on the reverse transformation matrix using the same criteria. The overlay factor can be calculated by:  $O(x) = direction \cdot (\# \text{ of overlapped voxels} - 1)$ , where  $direction = 1$  if shrinkage and  $direction = -1$  if expansion. The  $O(x)$  map was smoothed by Gaussian kernel and color-coded to illustrate the spatial shrinkage/expansion pattern.

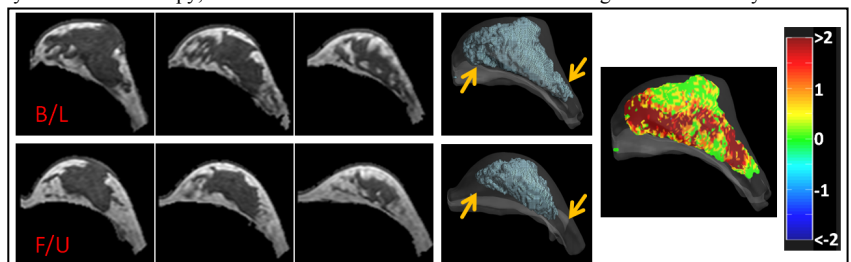
### Results:

Three case examples are shown. **Figure 1** shows a young (32 year old) patients who has extremely dense breast and shows severe density atrophy after receiving chemo. The quantitative dense tissue volume was 190 cc at baseline and 116 cc at follow-up scan, showing 39% reduction. The shrinkage of breast density can be easily observed on original images by visual inspection. The 3D rendering view of the density inside the breast clearly demonstrates that the most noticeable change is at the medial and lateral sides (by arrows). The value of overlay factor  $O(x)$  in **Fig.1** ranges from -7 to 50 with the absolute mean = 4.1. It can be seen that a large posterior area shows a severe shrinkage, with overlay factor greater than 2 (that is, more 2 voxels at B/L collapse into one voxel at F/U). **Figure 2** shows an older woman (41 years old) who has a moderate breast density. She also shows decreased fibroglandular tissue volume, from 116.3 cc at B/L to 110.3 cc at F/U, with 5.2% reduction. The value of overlay factor  $O(x)$  in **Fig.2** ranges from -9 to 5 with the absolute mean = 0.64. On the spatial shrinkage map, it can be seen that only some scattered regions have overlay factors greater than 2 (coded by red color). **Figure 3** shows the change in a healthy volunteer between 2 MRI scans done at 1 week apart. The fibroglandular tissue volume is 36.6 cc at B/L, and 35.9 cc at F/U, only showing 1.9% difference. The value of overlay factor  $O(x)$  in **Fig.3** ranges from -1 to 3 with the absolute mean = 0.15. The spatial registration map is mostly coded by green, and the results indicate that there is very little change.

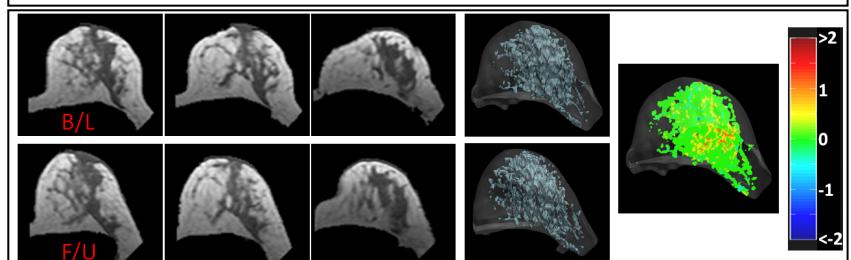
### Discussion:

We have implemented a registration method based on rigid alignment followed by non-rigid Demon's algorithm for analysis of changes in breast density, and demonstrated that the number of collapsing voxels at each spatial location during transformation can be used to illustrate the spatial change pattern. The results were consistent with quantitative % volumetric reduction of density and visual inspection findings. In the selected case examples, the tool reveals the atrophy caused by chemotherapy, and shows very little change between two scans of normal volunteers. Further refinements of this method may provide a useful tool for evaluating density changes in screening breast MRI of high-risk women to help radiologists detect early abnormalities by comparing to prior MR scans.

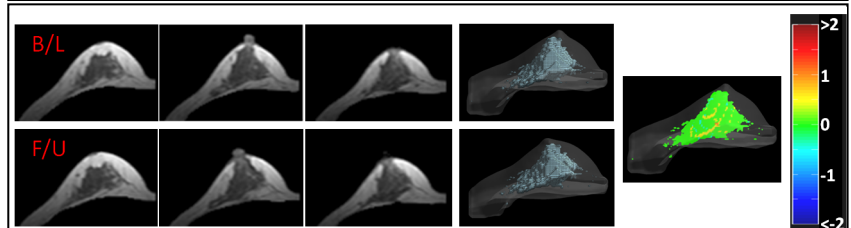
**Ref:** [1] Nie et al. Med Phys 2008;35(12):5253-5262. [2] Sled et al. IEEE Tran Med Imag 1998;17(1):87-97. [3] Thirion Med Imag Anal 1998;2(3):243-260. [4] Kroon et al. IEEE Intl Symp on Biomed Imag 2009;963-966. **Acknowledgement:** This work was supported in part by CBCRP 16GB-0056.



**Fig.1:** One example from a 32-year-old patient receiving neoadjuvant chemotherapy, who shows a severe breast atrophy with 39% reduction in fibroglandular tissue volume at F/U after receiving chemo compared to pre-treatment B/L. Column 1-3 show images from 3 different levels. The shrinkage of density can be recognized by visual inspection. Column 4 shows the 3D rendering of fibroglandular tissues inside the breast. The shrinkage is mostly noticeable in medial and lateral sides (by arrows). The last column shows the spatial shrinkage pattern of fibroglandular tissues determined by registration using Demon's algorithm. Warm colors indicate density shrinkage; green color indicates no change.



**Fig.2:** One case example from a 41-year-old patient receiving neoadjuvant chemotherapy who shows 5.2% reduction in fibroglandular tissue volume at F/U compared to B/L. The density shrinkage cannot be recognized by visual inspection. Column 4 shows the 3D rendering of fibroglandular tissues inside the breast, but the difference in the shape of the breasts between these two scans make assessment of shrinkage pattern difficult. The spatial shrinkage pattern shown in the last column indicates that some areas are showing shrinkage of fibroglandular tissues, but the degree is much less compared to Fig.1.



**Fig.3:** One case example from a normal 48-year-old volunteer who received two MRI scans one week apart. The quantitative measurements show that the dense tissue volume measured at F/U is 1.9% different from that of baseline. There is no discernable difference that can be picked up by visual inspection. The spatial registration map shows green color in the entire space, indicating no change.