Breast MR Registration for Evaluation of Neoadjuvant Chemotherapy Response

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Purpose

MRI has been proven as the most sensitive imaging modality for evaluation of neoadjuvant chemotherapy response in breast cancer patients [1]. Unlike clinical examination, mammogram or ultrasound, the residual tumors could be evaluated based on 3-D tomographic MR images. Following a baseline scan to assess pre-treatment tumor location, size and extent, multiple follow-up scans are conducted during the course of chemotherapy to monitor the changes. Due to the deformable nature of the breast, it is difficult to match the shape of breasts between baseline (B/L) and follow up (F/U) scans, particularly when the tumor is shrinking. The most challenging problem may be in patients with multi-focal or multi-centric lesions. Furthermore, it is common for patients to develop therapy-induced inflammation (mastitis), which also shows contrast enhancements. If the location of mastitis is very close to the tumor site, it may be mistaken as residual disease. In this study we developed a method for co-registering the B/L and F/U scans, to precisely pin-point the location of baseline tumors in follow-up scans and hence allow an accurate assessment of the therapy response. It is also desirable that tumor volumes be maintained during the transformation.

Methods

B/L scan forms the target volume that will be re-formed to match the F/U reference scan. The algorithm consists of a two-step process. Rigid registration of B/L and F/U scan aligns the two volumes in the vicinity of each other. A non-rigid registration algorithm [2] based on B-splines is then employed to further compensate for the non-linear differences between the two volumes. The extent of registration is measured by the normalized correlation between the two sets. While the scan parameters have been maintained at best between the serial studies, using the normalized cross-correlation constraint ensures that any intensity variations will be accommodated and will not affect the outcome of our algorithm. An additional constraint is imposed on the non-rigid transformation to maintain the tumor volume between transformations. Since non-linear warping can cause tumor volume to grow or shrink leading to incorrect assessment of tumor change due to chemotherapy, we restrain the tumor size by imposing a rigidity constraint on the tumor sub-grid, i.e. the B-spline control points engulfing the tumor are maintained equidistant throughout the registration process. Tumor volume, V was computed by determining the area of the ROI (manually selected) pertaining to the tumor, in each slice that the tumor was visible.

Results

Figure 1 shows a patient with multi-centric lesions. The F/U scan was taken 42 days after she completed 2 cycles of treatment. The patient had an index lesion of size 3.1 cm and several other smaller lesions ranging from 0.6 to 1.5 cm. Four lesions are demonstrated in row 1 as strongly enhanced areas on subtraction images. The slice number increases from superior to inferior, and each slice is 4 mm thick. The index lesion is the large mass shown on slices-15, 16 and 20. Three smaller lesions are shown on slices-10, 12 and 20 (posterior to the index lesion, close to the chest wall). Row-3 shows the transformed B/L images obtained by warping the B/L scan to match the shape of the F/U scan (row-4). This leads to precise localization of individual tumors. As can be seen by change in tumors sizes at corresponding locations, the patient was showing a great response to chemotherapy. The index lesion is now reduced to 1.0 cm while the smaller lesions are almost non-existent at the corresponding site. The relative tumor size changes between the B/L scan and its reformed version were measured for quantitative analysis of our registration process. The results indicated that the constraint of tumor volume preservation was working reasonably well with an accuracy of an average of 5-pixel difference. Thus, the algorithm allows transformation of images to match that of a reference set, while preserving the tumor size. Figure 2 shows a patient with a single large lesion. After 4 cycles of chemotherapy, the F/U scan showed some enhancement at a farther location from B/L tumor site. Registration of B/L with F/U scan also captures the relative spacing, indicating a case of therapy-induced inflammation. Histological examination of the enhanced area supported this evaluation.

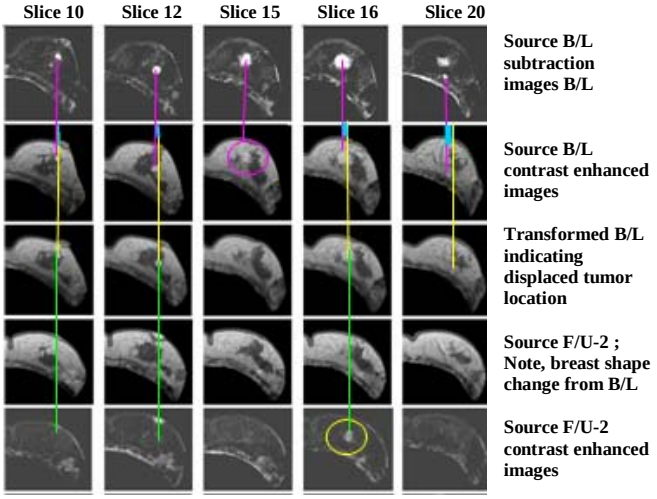

Figure 1: Transformation of B/L to F/U-2 helps in precisely locating the previous tumor sites. Thickness of blue line represents the mis-registration between centroids of multi-centric tumors due to shape variations. After transformation of B/L (row 3), we have a precise correlation as seen by the merging of yellow and green lines representative of extensions of tumor centroids. Small tumors disappear after chemotherapy; single large tumor is shrinking in size as noted by its absence on slice 15& 20, and reduced size on slice 16.

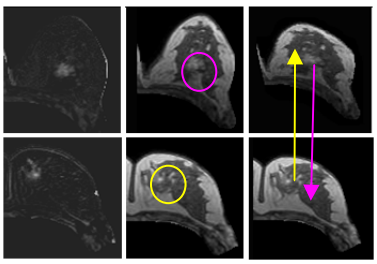

Figure 2: Enhancement seen in F/U-2 (row 2) is most likely due to mastitis, because transformation of F/U-1 to F/U-2 (row 1, col. 3) shows ample spatial difference between the two enhancements. Pink and yellow arrows indicate probable locations of F/U-1 and F/U-2enhancements.

Discussion

We have described and demonstrated non-rigid registration techniques with tumor shape and volume preservation constraints to assess neoadjuvant chemotherapy response in patients with multi-centric and multi-focal lesions. By warping the B/L scans to match the follow-up images we can precisely pin-point the previous tumor sites. The tumor shape and volumes were preserved to within 8% accuracy. This number may be attributed to the manual tracing of tumor outlines which are subjective. The algorithm is expected to be very helpful to evaluate mastitis-appearing lesions, to confirm that they are not part of residual disease, but from a normal tissue area based on transformed pre-treatment images.

References: [1] Martincich L. et al, Journal of BCRT, Vol. 83, 2004, pp. 67-76. [2] Rueckert D. et al, IEEE TMI Vol 18, No. 8, 1999 pp. 712-721.

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