

Registration between MRI and spot mammograms: results and applicability for X-ray guided biopsy of MRI only lesions

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ABSTRACT

Breast cancer is the most common type of cancer among women worldwide. Contrast-enhanced magnetic resonance imaging (CE-MRI) is routinely used to find suspicious lesions in breasts, which are not visible on mammography. These lesions need to be further evaluated using an MRI-guided biopsy. MRI-guided biopsy is not available everywhere, and it is expensive and time-consuming. A novel method was proposed in our earlier work for matching between magnetic resonance imaging (MRI) and spot mammograms. Having such a method would allow biopsying lesions, which are only visible in MRI, by the widely available and cheaper X-ray guided biopsy. Two registration methods have been developed to achieve this goal: a biomechanical model-based registration between MRI and full X-ray mammograms, followed by an image-based registration between full and spot mammograms. In this paper, we focus on evaluating the cumulative registration of the two methods using 51 patients from the Medical University of Vienna. We also simulate and assess whether the biopsy needle hits the predicted position of the lesion. The median target registration error (TRE) achieved is 35.6 mm . For 11 or 14 of the 51 datasets, an X-ray guided biopsy would be successful when extracting 12 or 24 specimens with a standard needle biopsy, respectively.

Keywords: X-ray guided breast biopsy, MRI, biomechanical model based registration, Clinical use

1. INTRODUCTION

In 2020, 15.5% out of women affected by cancer worldwide died from breast cancer.¹ Screening with X-ray mammography is key for early diagnosis. Depending on many factors, X-ray mammography however may miss detecting suspicious lesions. Thus, alternative imaging modalities such as magnetic resonance imaging (MRI) can be used to identify these lesions, since it is considered the most sensitive imaging method.² However, MRI-diagnosed lesions could cause a problem in clinical workflow, since malignancy is discovered in every second to a third of these types of lesions.^{2,3} Hence, further follow-up or MRI-guided biopsy is required. MRI-guided biopsies are costly, not widely accessible, and require a long time to perform the biopsy procedure.⁴

We previously proposed a novel approach to solve this problem: Instead of using MRI-guided biopsy, X-ray guided biopsy could be used by transferring the position of the lesion that is only identified in MRI to spot mammograms, which are acquired during X-ray guided biopsy, using image registration methods.⁵ The proposed method consists of two registration steps: a biomechanical model based registration between MRI and X-ray mammograms,^{6,7} followed by an image based registration between full X-ray and spot mammograms.^{8,9} Both methods have been tested and evaluated using clinical datasets, yet only one dataset has been used until now to assess the feasibility of the cumulative registration.⁵

In this paper, we focus on the evaluation of the cumulative registration of the two proposed registration methods using a total of 51 clinical datasets. We also evaluate the correlation between the accuracy of our method and the characteristics of patients. Furthermore we present methods to simulate an X-ray guided biopsy given the lesion position in the MRI to analyze whether the method could be clinically used.

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2. METHODS

This work builds on the previously developed methods.^{5,8,9} In order to transfer the position of a lesion from an MRI volume to the spot mammogram taken during X-ray guided biopsy, two image registration steps are applied: first the MRI is aligned with the full X-ray mammogram by a biomechanical model based registration, second the full X-ray mammogram is aligned with the spot mammogram by a rigid image based registration.

The biomechanical model registration uses the patient-specific geometry of a 3D MRI to predict a configuration of the breast that is similar to its shape in X-ray mammography. For this purpose, the MRI volume is automatically segmented into fatty, glandular and muscular tissue.¹⁰ Subsequently, a tetrahedral meshing is applied to create the geometric model of the breast. By assigning material properties and boundary conditions, a FEM simulation is described, which is used to virtually replicate the mammographic deformation to the MRI. The biomechanical model accounts for the non-linear and incompressible deformation of the breast. The image based registration consists of three steps: pre-processing, determining a region of interest (ROI) from the full X-ray mammography, and applying image similarity metrics between the ROI and the spot mammogram. To make the method robust, different image similarity metrics are combined and clustered using K-means. A rigid transformation between the two images is assumed.

Combining these two registration methods leads to the results which we refer to as cumulative registration in this paper: the lesion position is tracked from the MRI to the full mammogram using the computed deformation field of the FEM simulation. Then the predicted lesion position in the X-ray mammogram is tracked to the spot mammogram by the transformation found in the image based registration step and finally serves as a virtual target for the biopsy.

To analyze the clinical applicability of this approach, we mimic what would happen if a biopsy needle was inserted at the predicted position of the lesion location in the spot mammogram. The objective is to determine whether the biopsy needle hits the actual lesion. The size and dimensions of the needle used at the Medical University of Vienna were modeled to conduct this inquiry. Radiologists reported collecting 12 or 24 specimens using a 9-gauge vacuum-assisted biopsy device. They also approximately estimated the tissue biopsy area, which can be approximated by a cylinder around the needle's main axis. According to the biopsy compression views, this can be seen as a circle for needle biopsies performed perpendicular to the compression paddle (Figure 2 c), or as a rectangle for needle biopsies performed parallel to the compression paddle (Figure 2 d). For the circle shaped region, the estimated biopsy area for 12 and 24 specimens was of radius 15 mm and 25 mm, respectively. For the rectangular shaped region, the estimated biopsy area was $20 \times 10\text{mm}$ and $30 \times 20\text{mm}$, respectively. We then assessed if this area overlaps with the annotated lesion in the spot mammogram.

3. RESULTS

We tested our methods using 51 patient datasets from the Medical University of Vienna. The dataset consisted of a full set of MRI images taken with and without contrast agent on a Siemens 3T Trio Tim device, a full field digital cranio-caudal view (CC) and medial-lateral oblique (MLO) mammogram taken from a variety of devices, and a spot mammogram taken during an X-ray biopsy on a Fischer table or on the mammography device directly, i.e. in prone or upright position respectively. Spot mammograms were either taken in cranio-caudal, medio-lateral (ML) or lateromedial (LM) view. Image pairs for the image-based registration between the full X-ray mammogram and the spot mammogram were selected based on the view in the spot mammogram: for CC spot mammograms, a matching CC full mammogram was used. For ML or LM spot mammograms the MLO full mammogram was used, neglecting the difference of 45° in view angle.

As a landmark to assess the target registration error (TRE), the centers of gravity in each modality of freehand lesion annotations have been calculated. The annotations of corresponding lesions have been performed by an expert radiologist using 3D Slicer¹¹ in the MRI volume, the full X-ray mammogram and the spot mammogram.

The predicted annotation positions derived from the MRI annotation and annotations carried out in the full mammogram were used to compute the TRE, true positive rate (TPR), intersection over union (IoU), and dice coefficient (DSC). These metrics assess the accuracy of the biomechanical based registration. Similarly, the accuracy of the image based registration between full X-ray mammogram and spot mammogram was evaluated. Finally, the total TRE, TPR, IoU, and DSC were calculated by comparing the predicted position in the spot

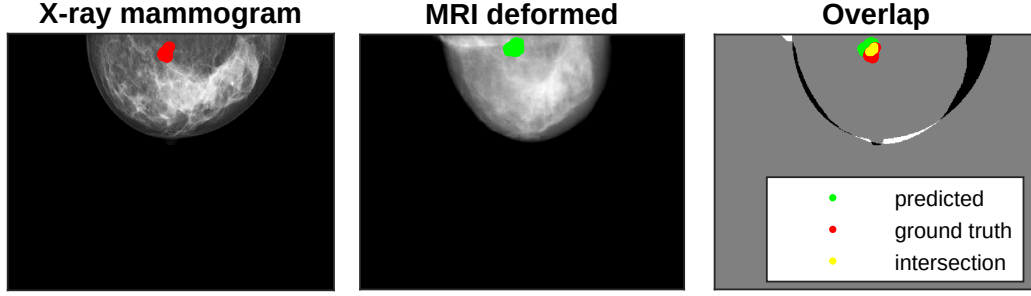


Figure 1. An example of registration between MRI and X-ray mammography using biomechanical model based registration: original X-ray mammography (first), synthetic X-ray (second), overlap of the two images (third). Ground truth annotation marked by radiologists in the original X-ray (red), projected tracked annotation of the MRI into the synthetic X-ray (green), and overlap between the two lesions (yellow).

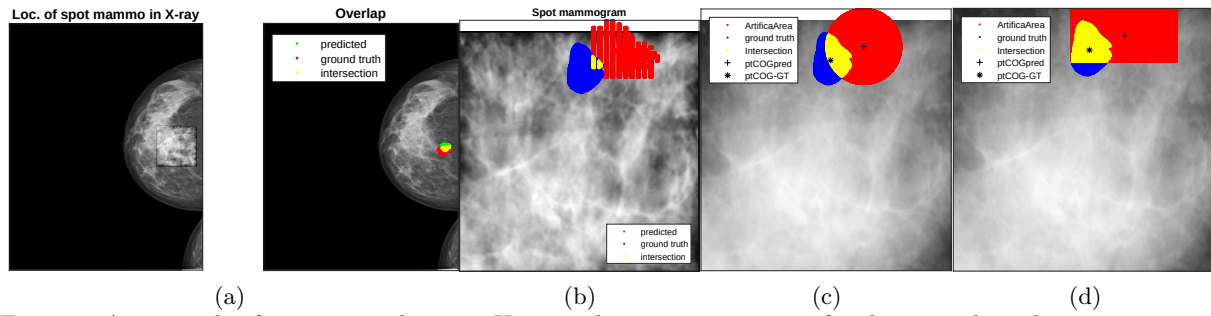


Figure 2. An example of registration between X-ray and spot mammograms for the same showed case using image based registration (a): location of spot mammogram in full X-ray mammogram (left). Overlap between the lesion annotated by radiologists in the original X-ray (red), prediction of the position of the lesion (green), and overlap between the two lesions (yellow) (right). An example of the accumulative registration (b). An example of a successful biopsy that could be used clinically based on the predicted area (red). Blue represents the annotation of the lesion in the spot mammogram and yellow represents the overlap of both. CC direction, issued will be excised in an area of 15 mm diameter (c), and ML direction, issued will be excised in an area of 20 × 10 mm (d).

mammogram using the cumulative registration to the ground truth marked by radiologists in the spot mammogram. The individual registration methods achieved a median TRE of 31.8 mm and 20.2 mm for the MRI to full X-ray mammogram registration and the full X-ray mammogram to the spot mammogram registration, respectively. The number of overlapping annotations of the lesions after registration is 22 and 26 cases, respectively. An exemplary result of the registration between MRI and full X-ray mammography is illustrated in Figure 1. An exemplary case of the registration between full X-ray mammogram and spot mammogram is shown in Figure 2 a and b.

The cumulative registration of the two methods achieves a median TRE of 35.6 mm, as shown in Figure 4. The lower and upper quarters are 20.7 mm and 49.5 mm, respectively. The minimum and maximum errors are 5.7 mm and 106.1 mm. For cases with high errors, like the maximum reported, e.g. 106.1 mm, the error in both individual registration methods is high. The individual TREs are 43.2 mm and 67.3 mm. Hence, the two errors add up in this case.

Further analysis of the cases showed that biomechanical model based registration especially for X-ray mammograms taken in MLO projection tends to have a higher TRE. More optimization in rotation angle and positioning of plates could help those cases to decrease the errors in future. In the image based registration we recognized a tendency that our approach may be slightly over-fitted to the contrast of an X-ray mammography device which provided the majority of the cases. For X-ray mammograms taken on device with few cases in our dataset only, the TRE tends to be higher. In future we would like to address this issue by increasing our database and revisit the parameter optimization of the image based registration.

With respect to the intersection between the two annotations, the three metrics show an overlap for 18 cases out of the 51 patients as shown in Figure 3 for the cumulative registration. The maximum DSC achieved is 0.45. For 14 of 51 patients a biopsy would be successful: in those cases the simulated biopsy area overlaps with the annotated ground truth in the spot mammogram. One limitation of our method is that the biopsied area is centered around the center of gravity of the annotation made in the MRI. Depending on the shape of this freehand annotation, the center of gravity may be an in-optimal reference position. Selecting a target position based on the lesion shape would be an option we consider to include in future.

For all 51 cases we performed a sub-group analysis by correlating the registration accuracy with several dataset and patient characteristics. The results showed that the registration accuracy does not correlate with patient age, density of breasts, breast sizes, and lesion sizes (first degree polynomial fit: $r=0.09$, -0.036 , 0.041 , and -0.18 , respectively). The accuracy correlates with the mammographic views: cases in which the view in the full X-ray mammograms and spot mammograms are different (e.g. MLO/ML) show a higher TRE. Moreover, the accuracy correlates with the locations of lesions in the three modalities: the accuracy is better for more central lesions.

4. DISCUSSION AND CONCLUSION

We presented a follow-up study for the earlier proposed method to align MRI volumes with spot mammograms. We evaluated 51 clinical datasets from clinical routine. A limitation of the available data is that it only contains cases with lesions visible in all modalities for evaluation reasons. While not being used for registration explicitly, a clinical use case would be different since the purpose is to apply this method for patients with lesions not visible in X-ray mammography and spot mammograms. It remains to be investigated if the proposed methods are affected by that, for example in solving the image based registration.

Additionally to our previous work, a needle biopsy based on the cumulative registration from MRI to X-ray mammograms and from X-ray mammograms to the spot mammograms taken during X-ray guided biopsy was simulated to analyze in which cases the method would lead to a successful biopsy and would thereby be applicable for the intended clinical use case. Though only 14 out of 51 patient could be successfully biopsied, we believe the proposed methods showed promising results and a basic feasibility for clinical use: we could already show that for certain patient characteristics our approach has a higher success rate than on average, e.g. for central lesions and if the views in full X-ray mammogram and spot mammogram match. The methods are however independent of age, histopathology, breast density, breast sizes, and lesion sizes. This is considered a positive property since the method can be applied to a lot of variances in the characteristics of the patients and pathologies. An advantage of our method is that all images can be acquired by common devices and protocols without the need for special equipment like compression paddles for MRI.

The two individual registration steps can generally be used independently. Yet our results show that the biomechanical model based registration between MRI and full X-ray mammograms shows a slightly higher TRE than the image based registration between full X-ray mammograms and spot mammograms. This could be expected since the breast deformation between the modalities is considerably higher between MRI and X-ray mammography due to the imaging position in prone position (MRI) and fixed between compression paddles (X-ray mammography). We furthermore showed that the errors of both registration steps may add up, which leads to a large error for the cumulative prediction of the lesion position in the spot mammogram. There are several approaches to reduce the TRE for the biomechanical model based registration in future: first, a parameter optimization like it was applied in our previous work¹² may be applied to considerably reduce the error. Second, it would be interesting to enhance the methods for tomosynthesis-guided biopsy (3D) to eliminate the projection to 2D, opting instead for a direct transition from 3D to 3D. For this purpose adaptations of the method applied in our previous work¹³ could be incorporated into the current work.

Together with the identified challenges and limitations of the individual registration methods that were pointed out (e.g. over-fitting to X-ray mammography contrast of certain devices), we have gained insights into potential future improvements that may lead to a considerably higher success rate. In the future, the method could enable performing a widely accessible and less expensive X-ray guided biopsy, even if a suspicious lesion can only be seen in an MRI.

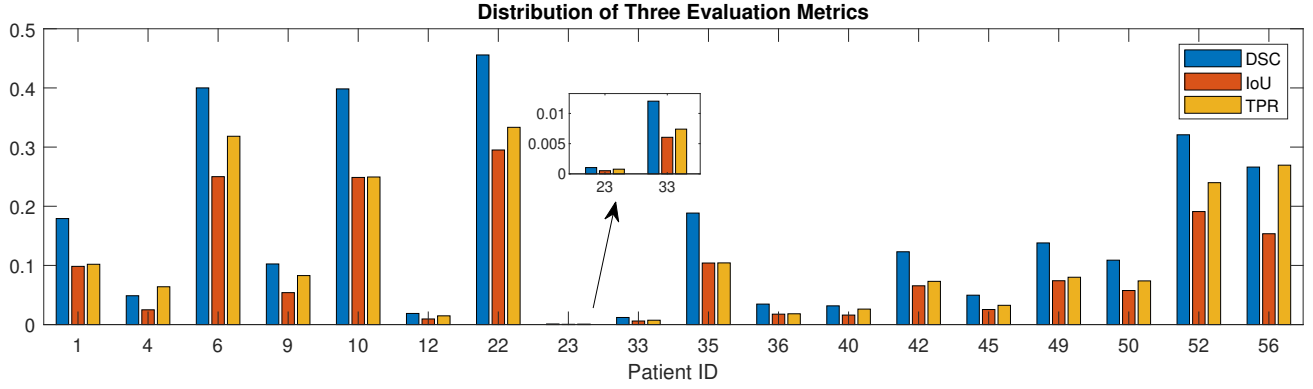


Figure 3. Distribution of the three evaluation metrics for the intersection between the actual and the predicted lesion for the accumulative registration. 18 out of 51 cases achieve an intersection between the two annotations.

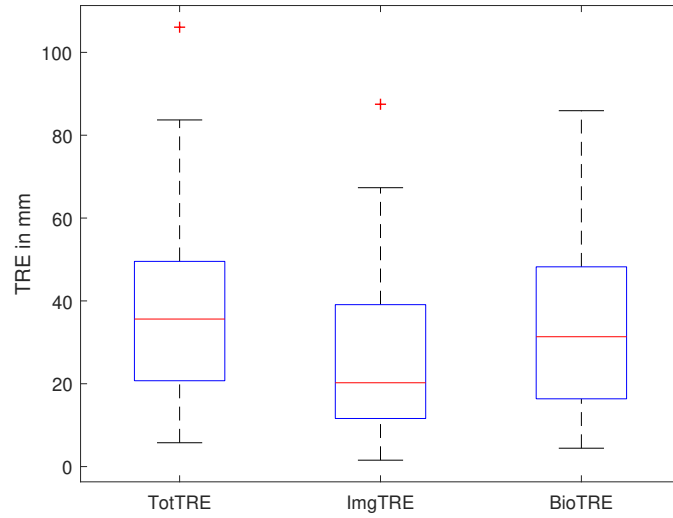


Figure 4. Analysis of TRE of the cumulative registration of the two methods (denoted as TotTRE), the image based registration (denoted as ImgTRE), and the biomechanical model based registration method (denoted as BioTRE).

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