Evaluating Impacts of Motion Correction on Deep Learning Approaches for Breast DCE-MRI Segmentation and Classification

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Abstract. Dynamic Contrast Enhanced-Magnetic Resonance Imaging (DCE-MRI) is a diagnostic method suited for the early detection and diagnosis of cancer, involving the serial acquisition of images before and after the injection of a paramagnetic contrast agent. Dealing with long acquisition times, DCE-MRI inevitably shows noise (artefacts) in acquired images due to the patient (often involuntary) movements. As a consequence, over the years, machine learning approaches showed that some sort of motion correction technique (MCT) have to be applied in order to improve performance in tumours segmentation and classification. However, in recent times classic machine learning approaches have been outperformed by deep learning based ones, thanks to their ability to autonomously learn the best set of features for the task under analysis. This paper proposes a first investigation to understand if deep learning based approaches are more robust to the misalignment of images over time, making the registration no longer needed in this context. To this aim, we evaluated the effectiveness of a MCT both for the classification and for the segmentation of breast lesions in DCE-MRI by means of some literature proposal. Our results show that while MCTs seems to be still quite useful for the lesion segmentation task, they seem to be no longer strictly required for lesion classification one.

Keywords: Deep convolutional neural network · DCE-MRI · Breast · Cancer · Motion correction

1 Introduction

Breast cancer is one of the most common causes of death and a major public health problem worldwide. After skin cancers, it is the most diagnosed cancer among women, accounting for nearly one out of three. Researchers have identified hormonal, lifestyle and environmental factors that may increase the risk

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of breast cancer, but it's not clear why some people who have no risk factors develop it while other people with high-risk factors never do. Breast cancer is one of the most common cancers among women and still nowadays the key for reducing its death rate is early diagnosis: the later a tumour is diagnosed the more difficult and uncertain the treatment will be. To this aim, the World Health Organization (WHO) suggests mammography as the main breast cancer screening methodology for its fast processing and high diagnostic value [21] but, unfortunately, this methodology is not suitable for under-forty women (showing hyperdense glandular tissues).

In the last few years, researchers have been focusing on Dynamic Contrast Enhanced-Magnetic Resonance Imaging (DCE-MRI) as a complementary tool for early detection of breast cancer, demonstrating its potential both for staging newly diagnosed patients and in assessing therapy effects [6]. DCE-MRI advantages include its ability to acquire 3D dynamic (functional) information, not available with conventional RX imaging [24], its limited invasiveness, since it does not make use of any ionising radiations or radioactive contrast agent, and its suitability for under-forty women and for high-risk patients [1].

Consisting in the acquisition of multiple 3D volumes over time, DCE-MRI can be considered as 4-dimensional data (Fig. 1a), obtained by combining different images acquired before (pre) and after (post) the intravenous injection of a paramagnetic contrast agent (usually Gadolinium-based). As a consequence, each voxel (a three-dimensional pixel over time) is associated with a Time Intensity Curve (TIC) representative of the temporal dynamics of the acquired signal (Fig. 1b) that reflects the absorption and the release of the contrast agent, following the vascularisation characteristics of the tissue under analysis [23].

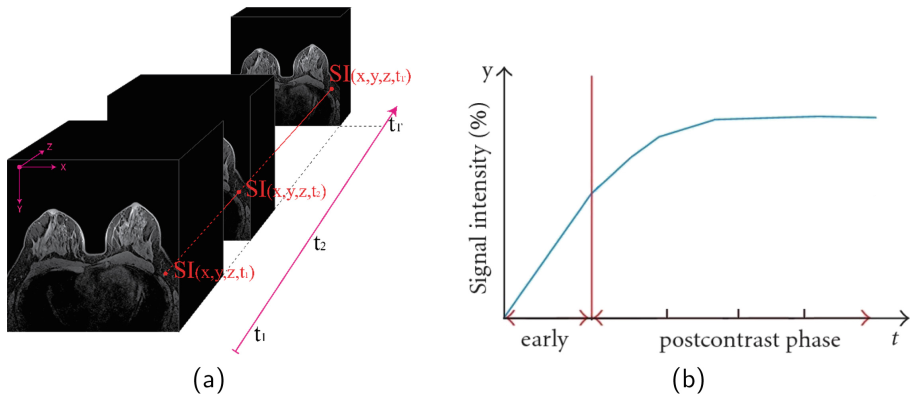

Fig. 1. DCE-MRI and Time Intensity Curves. (a) A representation of the four dimensions (3 spatial + 1 temporal) of a typical breast DCE-MRI. In red, an exemplification showing a voxel (of coordinates x, y, z) acquisitions over different time intervals (t_1 to t_T); (b) Illustration of a Time Intensity Curve for a voxel: the t axes represents the different acquisitions along time, highlighting the pre-contrast (early) and postcontrast injection phases; the y axes reports the acquired signal (and thus the voxel luminance) variation. (Color figure online)

While the use of DCE-MRI has proved to improve breast cancer diagnosis [8], it is a very time-consuming and error-prone task that involves analysis of a huge amount of data [11]. It follows that radiologist can hardly inspect DCE-MRI data without the use of a Computer Aided Detection/Diagnosis (CAD) system designed to reduce such amount of data, allowing them to focus attention only on regions of interest. Typical CAD system consists of different modules, each intended to address a given task, including lesion detection, segmentation and diagnosis. Although several papers propose the use of machine learning, still today it is not easy to identify the definitive set of features for an accurate lesion diagnosis and segmentation.

For this reason, several works explored the applicability of Deep Learning (DL) approaches in CAD system, in order to exploit their ability to learn compact hierarchical features that well fit the specific task to solve. CAD systems usually include some pre-processing stages intended to prepare data before the execution of the main phases, mainly in order to optimize image quality. Among them, Motion Correction Techniques (MCT) are used to face problems related to patient involuntary movements, such as breathing, that could introduce noise into the acquired images.

The aim of this paper is to analyze if deep learning based approaches are more robust to these small misalignments of images over time, reducing the need for MCTs. In particular, we evaluated the effectiveness of a MCT both for the classification and for the segmentation of breast lesions in DCE-MRI by means of some literature proposal.

The rest of the paper is organized as follows: Sect. 2 introduces MCTs; Sect. 3 describes the analyzed deep learning approaches, also introducing the considered dataset; Sect. 4 reports our experimental results; finally, Sect. 5 discusses the obtained results and provides some conclusions.

2 Motion Correction Techniques

One of the drawbacks of DCE-MRI is that, unlike other acquisition techniques, it can be very uncomfortable as it requires the patient to remain motionless throughout the whole acquisition time (tens of minutes). During this period, even small and imperceptible patient's movements (such as breathing) can introduce artefacts that could lead to incorrect DCE-MRI data analysis. To remove (or at least reduce) motion artefacts it is usual to apply a motion correction of the DCE-MRI volumes prior to any data analysis (e.g. lesion segmentation or detection) [22]. In this context, the aim of a Motion correction Technique (MCTs) is to re-align each voxel in the post-contrast images to the corresponding voxel in the pre-contrast (reference) image (Fig. 2), trying to maximize an objective function that is assumed to be maximal when the images are correctly aligned. In literature, several MCTs have been proposed [22,25], some of which have been adapted to be used in diagnostic medical imaging. Many surveys on motion correction agree in categorizing the techniques on the basis of the type of transformation used to realign two images:

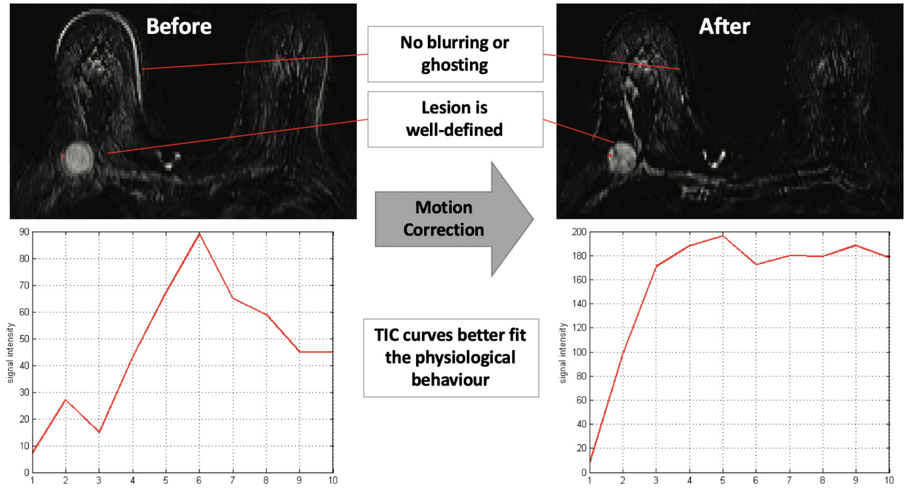

Fig. 2. Example of motion artefacts in a DCE-MRI Breast slice (upper images) and the TIC associated to the marked region (down images), before (left column) and after (right column) the application of a MCT.

- **Rigid/Non Rigid:** a rigid transformation (or affine) provides a set of transformations that include translations, scaling, homothety, similarity transformations, reflections, rotations, shear mapping, and compositions of them in any combination and sequence. Affine transformations are not able to model all possible anatomic deformations, especially those resulting in artefacts of soft tissues (i.e. breast), making elastic (non-rigid) transformations more suited in this cases [19]. Both rigid and elastic transformations can be applied on two-dimensional surfaces or on three-dimensional volumes [12].
- **Mono-modal/Multi-modal:** the term "modal" refers to the kind of scanner/sensor used to acquire the images. For multi-modal images, the correction technique aligns (register) images obtained from different scanners. The multi-modal registration is widely used in the medical field of complementary surveys such as CT/MRI brain and PET/CT total body [7].
- **Spatial or frequency domain:** The spatial methods operate in the domain of the image, by comparing the characteristics and/or the intensity pattern. On the other hand, in the frequency domain, it is possible to apply "phase correlation" methods which consist in rephrasing an image in relation to another. This phase-shift in the field of frequencies corresponds to an alignment that, unlike many algorithms in the spatial domain, is able to reduce the noise, the occlusion, and other defects typical of medical images.
- **Intensity or features based:** methods based on intensity rely on similarity measures that take into account the brightness values of each pixel/voxel. Feature-based techniques require targets images that, using some fixed points manually set or automatically determined, are used as the reference in the optimization process of minimizing the Euclidean distance between the image under correction and the target.

It is worth noticing that (i) many MTCs were not originally designed for medical imaging and (ii) that there is not a unique MCT that works best across different patients and different MRI protocols [9,14]. Moreover, MCTs are often very complex and their long execution time could make them not suitable to be used in a clinical context. As a consequence, many times simpler registration approaches are preferred, since they can usually perform as well as more complex ones, but requiring less computational effort [8,13].

An example of such approaches are median filters, a procedure that given a DCE-MRI image acquired at instant t, replaces each voxel v with the median value of the voxels in its neighbourhood (whose dimension depends on the size of the filter). Since (i) the strong computational requirement of DL approaches analyzed in this paper and (ii) the proved effectiveness of median filters as MCT in the breast DCE-MRI [15], in this work we consider the 3D Median Filtering approach, with a neighbourhood of 3 voxels along each projection (MEDx3).

3 MCTs and Deep Learning

In recent years, Deep learning (DL) approaches have gained popularity in many pattern recognition tasks thanks to their ability to learn compact hierarchical features that well fit the specific task to solve. Among these approaches, we can cite Convolutional Neural Networks (CNN) that are composed of different convolutional layers stacked in a deep architecture meant to automatically learn the best data representation. Their main characteristic consists in the fact that filters used for convolution operations are not known *a priori*, but are learned during the training stage. In other words, the network learns the best filters in order to create the best mapping between the set of inputs and the set of outputs. As a consequence, this characteristic results in no need for the feature extraction and selection phase. However, misalignment of images due to patient movement may still represent an open issue and, therefore, **the aim of this work is to be a first investigation on whether deep learning approaches are able to learn a set of features able to automatically mitigate the effects of motion correction artefacts**. To this aim, we evaluate the real effectiveness of MCTs for two deep models proposed in the literature, implemented respectively for lesion classification (diagnosis) and segmentation (detection). Both models have been re-implemented according to our best interpretation of the authors' papers and suitably evaluated to be fairly compared.

3.1 Lesion Segmentation

For the lesion segmentation task, we considered the use of a U-Shaped CNN, as proposed in [16] for the breast segmentation task. The approach consists of three main steps:

– Removing all the foreign tissues (bones, muscles, etc) and air background, by using an automatically segmented breastmask

– Extraction of *slices* by cutting the DCE-MRI 4D data along the axis with the highest resolution
– Slice-by-slice segmentation with a U-Net CNN.

The core of the approach is a U-Shaped CNN, an encoder-decoder architecture originally designed for biomedical electron microscopy (EM) images multi-class pixel-wise semantic segmentation [17]. Some modifications have been introduced in the original U-Net proposal: (a) the output feature-map of the network has been set to one channel to speed up the convergence during the training; (b) zero-padding with a size-preserving strategy has been applied for preserving the output shapes; (c) batch normalization (BN) layers after each convolution has been applied to improve the training stability.

3.2 Lesion Diagnosis

For the lesion classification task we considered the work proposed by Haarburger et al. [3] consisting in the use of a ResNet34 [4] CNN architecture pre-trained on the ImageNet dataset. The network is fine-tuned to work with breast DCE-MRI images and to face a binary classification problem (malignant vs benign lesions).

During fine-tuning on the DCE-MRI data, all layers are trained simultaneously using cross entropy loss (therefore no layers weights have been frozen). Moreover, since the network expects three input channels, a subset of the acquired images (T, see Fig. 1a) is needed. To this aim, authors provide an experimental comparison of all possible subset of images provided by the acquisition protocol and determine the best combination for malignancy classification.

3.3 Experimental Setup

Both CNNs have been implemented with the Keras high-level neural networks API in Python 3.6, by using TensorFlow (v1.6) as back-end for the U-Net CNN and Pytorch for the Haarburger et al. [3] work. The Python scripts have been evaluated on a physical server hosted in our university HPC centre equipped with 2 x Intel(R) Xeon(R) Intel(R) 2.13 GHz CPUs (4 cores), 32 GB RAM and an Nvidia Titan Xp GPU (Pascal family) with 12 GB GRAM.

The U-Net model for Lesion segmentation has been trained by minimizing a task-specific loss defined as follows:

$$\text{loss} = 1 - \text{DSC}(y_{\text{network}}, y_{\text{gold-standard}}) \tag{1}$$

$$\text{DSC} = (2 \cdot n(GS \cap SEG))/(n(GS) + n(SEG)) \tag{2}$$

where DSC represents the Dice Similarity Coefficient and $n(\cdot)$ represents the number of voxels in the enclosed volume. The network kernel weights have been initialized to random numbers from a standard distribution $\mathcal{N}(0, \sqrt{2/(\text{fan}_\text{i} + \text{fan}_\text{o})})$ [2] where fan_i and fan_o are respectively the input and output size of the convolution layer, while the bias weights have been initialized to a constant value of 0.1. ADAM optimizer [5] was used, with $\beta_1 = 0.9$, $\beta_2 = 0.999$ and $\text{lr} = 0.001$ using an inverse time decay strategy.

Haarburger et al. [3] network has been pre-trained on ImageNet dataset. Authors employed stochastic gradient descent using a momentum of 0.9, with a decaying learning rate starting at 0.001 and decreasing with a factor of 0.05 every 7 epochs.

3.4 Dataset

The dataset consists of 42 women breast DCE-MRI 4D data (average age 40 years, in range 16–69) with benign or malignant lesions histopathologically proven: 42 regions of interest (ROIs) were malignant and 25 were benign, for a total of 67 ROIs.

All patients underwent imaging with a 1.5 T scanner (Magnetom Symphony, Siemens Medical System, Erlangen, Germany) equipped with breast coil. DCE T1-weighted FLASH 3D coronal images were acquired (TR/TE: 9.8/4.76 ms; flip angle: 25°; field of view 370 × 185 mm × mm; matrix: 256 × 128; thickness: 2 mm; gap: 0; acquisition time: 56 s; 80 slices spanning entire breast volume). One series (t_0) was acquired before and 9 series (t_1–t_9) after intravenous injection of 0.1 mmol/kg of a positive paramagnetic contrast agent (gadolinium-diethylene-triamine penta-acetic acid, Gd-DOTA, Dotarem, Guerbet, Roissy CdG Cedex, France). An automatic injection system was used (Spectris Solaris EP MR, MEDRAD, Inc., Indianola, PA) and the injection flow rate was set to 2 ml/s followed by a flush of 10 ml saline solution at the same rate.

As **gold-standard** for the segmentation stage, an experienced radiologist delineated suspect ROIs using T1-weighted and *subtractive* image series. Starting from DCE-MRI acquired data, the subtractive image series is defined by subtracting t_0 series from t_4 series. In subtractive images, any tissue that does not absorb the contrast agent is suppressed. Manual segmentation stage was performed in Osirix [18], that allows the user to define ROIs at a sub-pixel level. All the lesion was histopathologically proven. The evidence of malignity was used as **gold-standard** for the lesion classification task.

4 Results

This section reports the results of the approaches described in Sect. 3 with and without applying the MEDx3 Motion Correction Technique. Performance is evaluated using a 10-fold cross validation, in turn using each fold for testing and the reaming ones for training and validation. In our case, if the fold i is used for testing, the previous one is then used for validation and all the other ones for training. It is worth noticing that, although each lesion is composed of different slices, the lesion diagnosis task has to predict a single class for the whole lesion. For this reason, **it is very important to perform a patient-based instead of a slice-based cross validation**, in order to reliably compare different models by avoiding mixing intra-patient slices in the evaluation phase.

Considering as the positive class the malignant one, segmentation performance are evaluated in terms of dice (DSC), Specificity (SPE) and Sensitivity (SEN), while classification performance are assessed in terms of Sensitivity (SEN), Specificity (SPE), F1-Score (F1) and Area under ROC curve (AUC).

Table 1 shows the results obtained by implementing U-Net for lesion segmentation with and without the use of the MEDx3 MCT.

Table 1. Results obtained by implementing the U-Net for lesion segmentation with and without the MEDx3 MCT.

	SPE	SEN	**DSC**
Piantadosi et al. [16]	100%	53.93%	**57.69%**
Piantadosi et al. [16] with MEDx3	100%	66.23%	**66.01%**

Similarly, Table 2 reports the results obtained by implementing Haarburger et al. [3] method without applying any MCTs and by applying the MEDx3 MCT. Since the network performs a slice-by-slice classification, a combining strategy is required in order to classify each lesion. As proposed in the original work [3], we aggregated all the lesion's slices predictions by taking the class of the slice with the maximum probability as the overall malignancy class for the lesion.

Table 2. Results obtained by implementing Haarburger et al. [3] model with and without the MEDx3 MCT.

	SPE	SEN	F1	**AUC**
Haarburger et al. [3]	42.86%	76.19%	71.11%	**70.75%**
Haarburger et al. [3] with MEDx3	50.00%	76.19%	72.73%	**69.73%**

Finally, since results with and without MC seems to suggest that lesions classification with DL approaches no longer needs a MC stage, for the sake of completeness, in Table 3 we compare the CNN performance with those obtained on the same task by using a non-deep approaches previously proposed in the literature [20], evaluating the performance in terms of AUC.

Table 3. Comparison in terms of AUC of CNN results with those obtained by using a non-deep approach.

	No Reg	MEDx3
Haarburger et al. [3]	70.75%	69.73%
Lavasani et al. [20]	65.31%	72.11%

5 Discussion and Conclusions

The aim of this paper was to carry a preliminary study in order to investigate if deep learning approaches are able to automatically mitigate the motion artefacts effects to the extent of making motion correction techniques no longer needed. We consider our previous work [8,13] where MEDx3, a simple MCT, was demonstrated to overcome the most advanced MCTs in the task of mitigating the artefacts in DCE-MRI breast images. All the evaluations are conducted with respect to the result in the tasks of segmentation and/or classification. Table 1 shows how MEDx3 can still effectively improve the performance of the lesion segmentation task that, therefore, still seems to be affected by the noise due to the patient's movements. On the other hand, Table 2 shows that the performance of Deep Learning based approaches for the lesion classification are not very impacted by the execution of a MEDx3 Motion Correction Technique. Therefore, in order to determine if this property is related on the task and not to the used MC approach, in Table 3 we compared the performance of the deep and of a non-deep approach, showing that in the latter case the use of MEDx3 can improve results up to 7%. These preliminary results seem to suggest that the lesion segmentation task can still be positively affected by the use of a simple MCT, that is MEDx3, while the lesion classification task is more robust to motion artefacts. A possible interpretation could be that while CNNs could learn motion invariant features for the diagnosis task, the need for a precise voxel-based segmentation can be strongly affected by the voxel misalignment over time. However, on the other ends, as already stated in [10], performance of current CNN for the lesion classification task are still no outstanding enough to sustain such a claim and, therefore, it is very important to push research in that direction.

As a final remark, we would like to highlight that a limitation of this study is the population size: our finding should be confirmed on a larger dataset. Moreover, in order to produce more general and robust claims, the effect of different MCTs should be analyzed. With this aim, future work will focus on exploring the effect of different MCTs on other deep approaches.

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