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4D co-registration of X-ray and MR-mammograms: initial clinical results and potential incremental diagnostic value

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ABSTRACT

Purpose: 4D co-registration of X-ray- and MR-mammograms (XM and MM) is a new method of image fusion. The present study aims to evaluate its clinical feasibility, radiological accuracy, and potential clinical value.
Methods: XM and MM of 25 patients were co-registered. Results were evaluated by a blinded reader.
Results: Precision of the 4D co-registration was "very good" (mean-score [ms]=7), and lesions were "easier to delineate" (ms=5). In 88.8%, "relevant additional diagnostic information" was present, accounting for a more "confident diagnosis" in 76% (ms=5).
Conclusion: 4D co-registration is feasible, accurate, and of potential clinical value.

1. Introduction

Breast cancer is the most frequent malignant neoplasm in women in the western world. Despite significant advances in therapy and diagnostic options, it is still associated with a high mortality [1]. Medical imaging is the only method to accurately detect this disease in a preclinical stage. Beside detection of the disease, medical imaging also plays a central role in the characterization of breast lesion (differential diagnosis: benign vs. malignant). Main radiological modalities used for this purpose are X-ray mammography (XM)—which might be complemented by breast ultrasound—and magnetic resonance mammography (MM) [2]:

XM is certainly the most commonly used breast imaging technique. Image contrast is mainly based on the electron density, and it generates classical projection images. Data acquisition is done in a standing position, and the breast is compressed during the examination. XM is a well evaluated diagnostic tool and allows to analyse topographic and morphologic characteristics of pathological findings. Notably, there are certain diagnostic features that can be imaged only by XM, including calcifications and microcalcifications [2].

As MM is a sectional imaging modality, it enables analysis of breast parenchyma without any overlap. It is performed in prone position without compression. During the examination, the breast is positioned in a dedicated breast surface coil. The physical basis of image contrast is completely different from XM and is based on magnetic tissue properties. Furthermore, MM is typically performed as a dynamic examination after the intravenous application of contrast agent. Accordingly, MM provides beside topographic 3D information additional functional data on tissue perfusion [3,4].

As both MM and XM show, to some degree, complementary diagnostic information, they are often read in combination. This is particularly important, as in most cases where an MM is performed, an XM will be available. However, accurate interpretation of MM requires high level of expertise, and topographic correlation of pathologies is difficult between both modalities. Such correlation requires high level of training and expertise, particularly due to the different geometric approach (projection vs. sectional image) and due to the deformation applied to the breast during XM.

To optimize this challenging task, automated co-registration solutions are desirable. This would allow the less experienced radiologist to more accurately and to more confidentially correlate both modalities. Furthermore, it is likely to speed up the combined reading with a subsequent benefit for workflow. However—not surprisingly—it is technically challenging to perform a co-registration and to transform the compressed projection images of XM into 3D MM or vice versa. Only few

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working groups have tried to solve this challenging task [5–7]. The approach developed by our team aims on a clinical application and, hence, tries to decrease operator interaction to a minimum, while maintaining a high level of automatization, for example [8,9].

However, similar to all concurrent approaches, it uses only morphologic information of MM. The functional information—for example, the dynamic enhancement data—is ignored. This is why we further developed the software and implemented functional data on tissue viability. For this, we implemented color-coded parametric maps of dynamic enhancement features into the registration algorithm. The resulting images combine the dimensional topographic and enhancement data of both modalities. Accordingly, we call this approach "4D co-registration" (4DcR). In an initial test, the technical feasibility of 4DcR could be demonstrated [10]. Yet, clinical evaluation by a breast radiologist is still pending.

Accordingly, this paper aims to analyse clinical performance, potential incremental value, and diagnostic impact of 4DcR.

2. Material and methods

2.1. Participants

Patients were randomly extracted from a database designed to investigate the co-registration of XM and MM: All patients received breast imaging at the Institute of Diagnostic and Interventional Radiology of the University Hospital Jena during a consecutive time period of 3 years (January 1, 2008 until December 31, 2010). This study was waived by the local ethical committee, and all patients gave written informed consent to the examination. Note that subgroups of this database have been used for previous investigations in different context, for example, Refs. [9,10].

All patients showed index lesions ≥10 mm being delineable in both imaging modalities. This criterion was necessary to assess overall accuracy (precision) of the co-registration. In order to avoid biological bias, time interval between XM and MM was restricted to a maximum of 2 weeks, and patients receiving breast treatment or intervention (biopsy, surgery, radiation therapy etc.) within this interval were not eligible.

2.2. Standard of reference

Final diagnosis was based on histopathological verification or long-term MM follow-up of at least 3 years. If follow-up scans initially rated as Breast Imaging Reporting and Data System (BI-RADS) II or I did not show any change, the lesions were classified as "benign".

2.3. Imaging methods

MR and XM examinations were supervised by one radiologists (Werner A. Kaiser) with high experience in breast imaging (XM and MM: >25 years of clinical experience) [11]. Standardized protocols were applied as follows:

Regarding technical specifications of MM, a full-field digital mammogram was acquired in standard projections [craniocaudal (cc), mediolateral oblique (mlo)] by a Hologic Lorad Selenia system. For MR image acquisition, standard clinical protocols according to international recommendations [12] were applied at 1.5 Tesla field strength (four channel receive only bilateral breast coils; Magnetom Symphony, Siemens Healthcare, Erlangen, Germany). Patient position was prone with axial scan orientation. Initially, eight spoiled dynamic T1-weighted gradient echo sequences (Fast Low Angle SHot, FLASH) were measured at 1-min intervals. After the precontrast scan, the contrast agent (Magnevist®, Bayer/Schering HealthCare, Leverkusen, Germany) was administered as a rapid bolus (3 ml/s) by an injector, intravenously (Spectris, Medrad, Pittsburgh, USA; dosage 0.1 mmol/kg). Postcontrast scanning started after a delay of 30 s. Technical parameters were 110 ms (repetition time), 5 ms (echo time), 80° (flip angle), 350 mm (field of view), 1.1*0.9*3 mm (in plane resolution), and 1 min (temporal resolution). In addition, a T2-weighted turbo spin echo sequence was acquired in identical slice position. However, this scan was not evaluated in this investigation.

2.4. Registration

Basic concept: The major challenge during the co-registration process is to accurately model the deformation of the breast during XM imaging. The basic idea is to simulate the deformable behaviour of the breast to achieve a compressed 3D MRI volume, which depicts the breast in the same configuration as during XM. We developed a semiautomatic software implementing a highly generalized model and, thus, requiring but one manual step. As neither knowledge on anatomic landmarks, tissue composition or the presence of pathologies is required, it can be implemented into clinical routine and might be handled by nonexpert radiologists or technicians [8,9].

3D co-registration: Based on the finite element method (FEM), the software mimics the compression during X-ray examination by creating an FEM mesh. For this purpose, a dedicated biomechanical model is used. It assumes incompressible material, that is, Poisson's ratio close to 0.5. Parameters are derived from a Neo-Hookean solid, simulating fatty tissue. Using Digital Imaging and Communications in Medicine (DICOM) Metadata (e.g., compression thickness), the contour of the breast (during X-ray examination) and the basic 3D volume (taken from the MRI scan), the software iteratively approximates an FEM model to fit the XM and MM. This generates a "deformed" FEM model allowing a pixel-by-pixel (or voxel, respectively) correlation of MM and XM data. Based on this deformed FEM model, it is then possible to create a "virtual XM." This can be compared to the original XM by various means, including the relative overlap of breast lesion [10,13].

4DcR: Beside morphologic and topographic data, MR mammography provides functional information on tissue vascularisation. These data are typically analyzed using T1-weighted scans before and after intravenous application of contrast agent [3,4]. In clinical routine, such information is usually categorized into the initial (precontrast vs. first minute postcontrast: washin) and delayed phase (first vs. last minute postcontrast: washout, plateau, and continuous increase) [14].

Previous investigations have shown that color coding of such enhancement characteristics might be beneficial for clinical routine [15,16]. We implemented this approach into the registration software: The initial phase was coded by brightness, whereas the delayed phase was coded by color [<10% (washout): red, −10% to +10% (plateau): green and >10% (continuous increase): blue]. According to our experience with the given scanner hardware and imaging protocol, we empirically defined an enhancement threshold at 30%.

Using this color coding approach, three-dimensional parametric maps based on the MM volume were created by the software. Such were further processed using the FEM mesh previously generated for 3D matching of the given breast. This enabled the creation of a second deformed FEM mesh implementing the "virtually compressed" parametric maps. Such were back projected on the original XM, resulting into the final 4DcR. The software was operated by an experienced user (Torsten Hopp). The whole postprocessing took approximately 30 min per dataset. Figs. 1 and 2 show examples of 4DcR as well as corresponding MM and XM. Further details of our 3D and 4DcR approach are beyond the scope of this paper and have been described in preclinical investigations, for example Refs. [10,13].

2.5. Image evaluation

One reader interpreted XM, MM, and corresponding 4DcR. He had intermediate experience in breast imaging (2000 examinations) and