European Journal of Radiology 106 (2018) 114–121

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Research article

Quantification of enhancement in contrast-enhanced spectral mammography using a custom-made quantifier tool (*I*-STRIP): A proof-of-concept study

M.B.I. Lobbes[a,c,*,1], H.K.P. Mulder[a,1], M. Rousch[b], W.H. Backes[a], J.E. Wildberger[a], C.R.L.P.N. Jeukens[a]

[a] Maastricht University Medical Center, Departments of Radiology and Nuclear Medicine, P.O. Box 5800, 6202 AZ Maastricht, The Netherlands
[b] Maastricht University Medical Center, Department of Pathology, P.O. Box 5800, 6202 AZ Maastricht, The Netherlands
[c] GROW School for Oncology and Developmental Biology, P.O. Box 616, 6200 MD Maastricht, The Netherlands

A R T I C L E I N F O

Keywords:
Mammography
Contrast-enhanced spectral mammography
Breast cancer
Contrast agent
Quantification

A B S T R A C T

Purpose: Contrast-enhanced spectral mammography (CESM) is diagnostically superior to full-field digital mammography. An important improvement for CESM would be the ability to quantify enhancement. In this proof-of-concept study we present a method for quantifying CESM enhancement.
Methods and materials: We developed a custom-made quantifier tool (*I*-STRIP) containing five chambers, each filled with a different iodine mass thickness (IMT). CESM grey values of the recombined image (CGV) in the *I*-STRIP were used to quantify breast IMT. We evaluated the *I*-STRIP's accuracy using a dedicated breast phantom containing chambers with known IMT's. Furthermore, we tested the effect of the *I*-STRIP on image quality and clinical use in five patients. Retrospectively, we studied whether current CESM protocols could distinguish between malignant and benign lesions in terms of CGV.
Results: Phantom experiments showed that quantification was independent of chamber height and size, phantom thickness and *I*-STRIP position for different IMT's (1.5, 3.0 and 7.5 mg l/cm^2). Near the phantom's periphery accuracy was found to be lower due to the breast-within-breast artifact. In the clinical setting (n = 5), workflow and image quality were not influenced by the *I*-STRIP. The mean IMT of these invasive breast cancers was 2.1 mg l/cm^2 (range 1.3–3.4 mg l/cm^2). Malignant lesions showed significantly higher CGV's than benign lesions (p = 0.002).
Conclusion: We showed in both phantom and clinical experiments that CESM quantification is feasible, without influencing workflow or image quality. The current CESM imaging protocol seems to be able to distinguish between benign and malignant breast lesions in terms of CGV.

1. Introduction

In 2011, the first commercially available contrast-enhanced spectral mammography (CESM, synonym: contrast-enhanced dual-energy mammography or CEDM) units became available. Currently, more and more vendors enter the arena with either prototypes or Food and Drug Administration approved devices. Since its introduction, many studies have shown that the diagnostic performance of CESM is superior to full-field digital mammography (FFDM) [1], matching or sometimes even surpassing the accuracy of breast magnetic resonance imaging (MRI) for breast cancer detection or assessment of disease extent [2–5]. CESM relies on uptake of circulating contrast agent (enhancement) in the tumor interstitium to acquire its high diagnostic accuracy.

In a typical CESM exam, an iodine based contrast agent is intravenously administered two minutes prior to the first (dual-energy) image acquisition. During image acquisition, a low-energy image is first

Abbreviations: AU, arbitrary units; *CA*-slab, contrast agent slab; CC, cranio caudal; CEDM, contrast-enhanced dual-energy mammography; CESM, contrast-enhanced spectral mammography; CGV, CESM grey value; FFDM, full-field digital mammography; IMT, iodine mass thickness; MLO, mediolateral oblique; MRI, magnetic resonance imaging; PMMA, polymethyl methacrylaat; ROI, region-of-interest; SD, standard deviation

* Corresponding author at: Department of Radiology and Nuclear Medicine, Maastricht University Medical Center, P.O. Box 5800, 6202 AZ Maastricht, The Netherlands.

E-mail address: marc.lobbes@mumc.nl (M.B.I. Lobbes).

[1] Both authors contributed equally.

https://doi.org/10.1016/j.ejrad.2018.07.021
Received 24 February 2018; Received in revised form 10 July 2018; Accepted 23 July 2018
0720-048X/

obtained, which is similar to FFDM [6]. This is immediately followed by the acquisition of a high-energy image which has no direct diagnostic value. Both images are used to reconstruct a recombined image [7], in which areas of enhancement are visualized. The low-energy and recombined images of both breasts, typically in two (standard) views, are available for the radiologist's assessment [8].

It is known from breast MRI that differences in contrast enhancement can be observed in different breast cancer subtypes. Consequently, multiple CESM studies have focused on the degree of enhancement on the recombined images to further standardize and improve the performance of CESM [5,9,10]. However, there is no consensus on how to rate the degree of enhancement. Therefore, various terms were introduced like 'yes/no', 'minimal', 'moderate', 'marked'. These terms are rather subjective (*i.e.* reader dependent) and do not support future comparisons of study results and optimization of CESM protocols. Hence, there is a need for a robust quantification method for rating enhancement of recombined CESM images.

In this proof-of-concept study, we aimed to evaluate a novel, custom made quantifier tool (*I*-STRIP) for use in CESM exams. As primary study objective, we evaluated the consistency of measurements of this tool in dedicated breast phantom experiments and tested its effect on image quality and clinical use in five breast cancer patients. As secondary study objective, we retrospectively evaluated whether current CESM protocols might be able to distinguish between benign or malignant breast lesions in terms of CESM grey value (CGV) measurements in the recombined images.

2. Materials and methods

2.1. I-STRIP

Together with Instrumental Development Engineering & Evaluation (IDEE, Maastricht, The Netherlands) we developed the *I*-STRIP, which is made of polymethyl methacrylaat (PMMA) and contains five circular chambers that can be filled with (iodinated) contrast agent with a concentration known to us (see below). Each chamber has a height of 0.3 cm and an area of 1.0 cm^2 corresponding to a diameter of 1.1 cm (Fig. 1). In this way, the *I*-STRIP could be used to translate the measured CGV in the breast (phantom) into an iodine mass thickness (IMT) in mg iodine per cm^2 (mg I/cm^2). The CGV reflects a measure for the contrast agent uptake (*i.e.* signal enhancement). CGV's cannot be translated into contrast agent concentrations (mg I/ml), since CESM images are two-dimensional projections of the breast (phantom). Hence, measured CGV's are converted into the IMT of a certain region-of-interest.

2.2. Breast phantom experiments

For the phantom experiments, the *I*-STRIP was placed next to a CIRS Model 020 BR3D Breast Imaging Phantom (Computerized Imaging Reference Systems, Inc., Norfolk, VA, USA) as shown in Fig. 1. This phantom consists of si x 1.02 cm thick semi-circular-shaped slabs. Each slab has a unique swirl pattern of two tissue-equivalent materials mimicking 100% adipose and 100% glandular tissue. In addition, a custom-made 0.52 cm thick contrast agent (*CA*)-slab of PMMA was developed (together with IDEE) and placed between the phantom slabs. This *CA*-slab contains 23 chambers which can be filled with (known concentrations of) contrast agent to simulate enhancing breast lesions. All chambers have the same height (0.3 cm), but three different areas to mimic different tumor sizes (0.2, 1.0 and 2.0 cm^2, corresponding to simulated breast lesion diameters of 0.5, 1.1 and 2.0 cm, respectively). The chambers were distributed near as well as far from the periphery of the breast phantom.

To verify that the CGV measured in the *I*-STRIP corresponded to the CGV measured in the breast (phantom), we performed phantom experiments in which the chambers of the *CA*-slab and the *I*-STRIP were filled with the same contrast agent (iopromide; Ultravist® 300 mg/ml, Bayer Healthcare, Berlin, Germany) used in clinical CESM exams. The five 0.3-cm high chambers of the *I*-STRIP were filled with 0 (*i.e.* solely demineralized water), 5, 10, 25 and 50 mg/ml of this contrast agent, corresponding to IMT's of 0, 1.5, 3.0, 7.5 and 15 mg I/cm^2. The *CA*-slab was filled such that each similarly-sized set of chambers was filled with

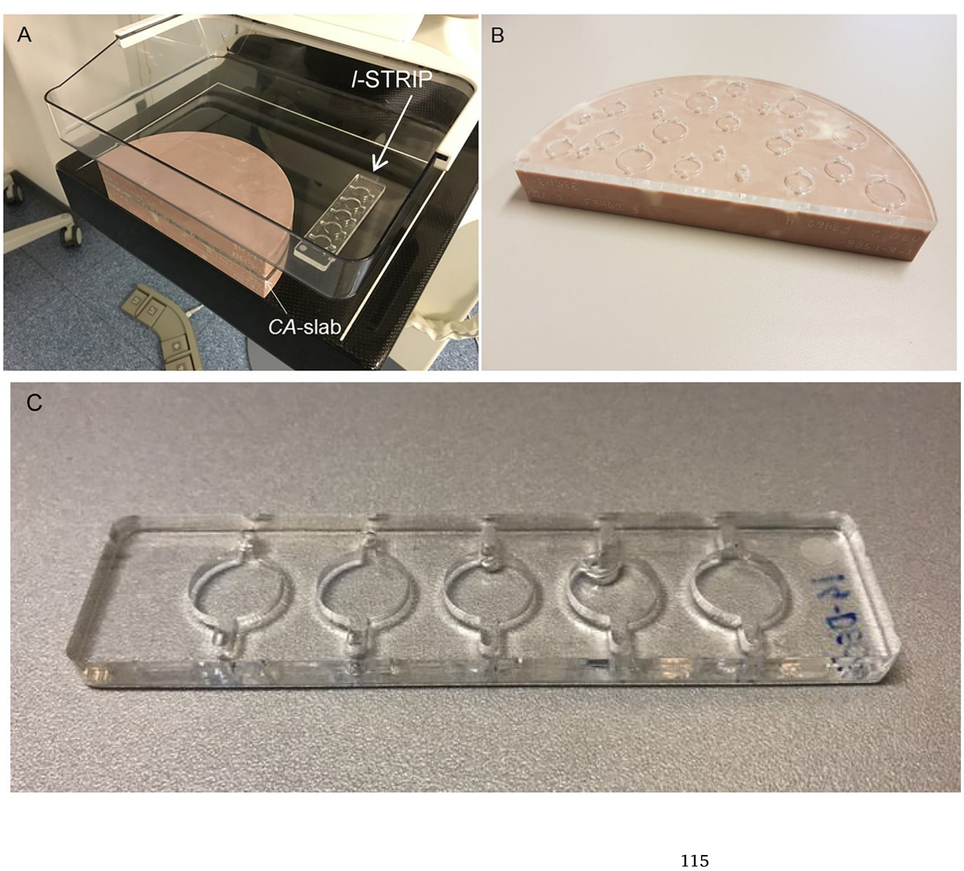

Fig. 1. A picture of the *I*-STRIP positioned on the mammography unit next to 4 slabs of the CIRS Model 020 BR3D Breast Imaging Phantom in between which the *CA*-slab was positioned at position number 3 (A, arrow) and the *CA*-slab placed on top of two slabs of the CIRS Model 020 BR3D Breast Imaging Phantom (B, arrow). Image C shows a detailed image of the *I*-STRIP.