Clinical Radiology xxx (2017) 1–8

Contents lists available at ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Factors affecting the precision of lesion sizing with contrast-enhanced spectral mammography

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ARTICLE INFORMATION

Article history:
Received 16 July 2017
Accepted 27 October 2017

AIM: To evaluate the precision of the pre-surgical measurement of the size of breast cancer by contrast-enhanced spectral mammography (CESM).

MATERIAL AND METHODS: This was a retrospective study of 204 breast cancers. Variables related to tumour biology and anthropometric variables were recorded and considered when evaluating the efficacy of CESM in predicting tumour size. Microscopic measurement of the largest diameter of the tumour at pathology was chosen as the reference standard.

RESULTS: The mean size of tumours at pathology was 20.7±15.8 mm, while at CESM it was 23.6±16.7 mm (Bland–Altman 2.9 mm overestimation, 2.9 mm; 95% confidence interval [CI]: −10.3–16.2 mm). Spearman's correlation coefficient was 0.83 ($p<0.0001$). The concordance analysis indicated that 37.8% of the measurements were concordant, 47% were overestimated, and 15.2% were underestimated. Tumour size, nodal involvement, breast density, and breast size significantly modified the sizing accuracy.

CONCLUSION: Quality of tumour size prediction with CESM is good, and this appears to be a promising imaging technique in the surgical planning of breast cancer. Biological tumour features, and anthropological characteristics of the patients do, however, affect the diagnostic precision and should be taken into account.

Introduction

Preoperative assessment of tumour size decisively influences the surgical recommendation of a radical mastectomy or conservative surgery, as well as deciding the volume of tissue to be resected, in order to obtain disease-free margins,[1–3] as incomplete or marginal tumour resection requires re-resection. It has been demonstrated that

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https://doi.org/10.1016/j.crad.2017.10.017
0009-9260/

pre-surgical tumour size prediction techniques that tend to underestimate the size of the lesions increase the risk of obtaining positive margins and consequently recurrence.[1,4] It is also important for oncologists because it allows them to make decisions regarding neoadjuvant chemotherapy.[5] Imaging technologies are therefore essential for preoperative assessment of breast cancer, and not only for diagnosis.

Mammography is a relatively imprecise technique for tumour sizing.[1,6] More accurate measurements are obtained with breast ultrasound (BUS),[1–3,7] and breast magnetic resonance imaging (MRI)[2,7,8]; however, MRI tends to overestimate actual tumour size, while BUS frequently underestimates it.[1,7] The role of newer imaging techniques in tumour sizing for preoperative planning is not clear in most cases.

Contrast-enhanced spectral mammography (CESM) is a promising diagnostic tool which combines the relative ease, low cost, and practicality of mammography with the high sensitivity of MRI.[9–13] CESM has been demonstrated to be consistently superior to conventional mammography, increasing diagnostic accuracy regardless of the reader's experience.[14] According to several studies, the sensitivity of CESM is high (>95%), the specificity is >65%, and the area under the ROC curve is approximately 0.85.[10,13,14] CESM uses intravenous contrast medium to obtain low- and high-energy images. The low-energy image is similar to a conventional digital mammography (DM). The high-energy image is used to form a "recombined image", which is obtained by subtracting the non-contrasted image, thus revealing the enhancing structures. The good specificity and sensitivity already demonstrated for CESM,[10,15,16] along with quickness and ease, make this technique an attractive alternative for surgical planning. In addition, many authors indicate that this technique might be cheaper than MRI (although more expensive than mammography and ultrasound),[12,17] but no cost-effectiveness studies are available to date for CESM.

To date, very few studies have evaluated the precision of the CESM for determining tumour size for surgical planning,[9,10,18] and there are still fewer available studies that have assessed in detail what factors affect precision. Therefore, the present study was undertaken with the double objective of establishing the precision of tumour sizing at CESM, and evaluating the biological factors influencing this precision.

Materials and methods

Patients and study design

In the San Roque Hospital Group, women without contraindications for the intravenous administration of an iodine-based contrast agent are eligible for CESM if they[1]: have palpable lesions[2]; a clarification of already identified abnormalities at mammography and/or BUS is required, namely mass lesions, areas of parenchyma distortion, focal asymmetries, or suspicious microcalcifications; or need further evaluation of heterogeneous dense breast parenchyma.[3] Since CESM was implemented in the hospitals in 2013, all patients have been informed that this is a novel technique and that their radiological data could be used in future scientific studies. Only those patients from whom written informed consent was obtained, according to a model previously approved by the ethics committee of the institution, were included in the database for scientific studies. Up to December 2016, this database contained 485 entries.

For this research, a retrospective search of the breast surgery and breast imaging databases was performed for patients who fulfilled three conditions[1]: they underwent CESM and signed the informed consent, and therefore were included in the database[2]; they had breast cancer surgery at the institution between August 2013 and December 2016; and a surgical specimen was obtained and its histopathological measurement was obtained. One hundred and fifty-eight patients (mean age 51.1±10.7 years, median 49 years) who underwent mastectomy (20.3%) or local excision (79.7%) were selected for inclusion. Twenty-six patients came from screening and 132 had palpable lesions. From these patients, a total of 204 malignancies were included in the study, because 32 patients had multifocal or multicentric breast cancers, and three patients had bilateral breast cancer. This research focused on the size of these 204 individual lesions, without considering multifocality or multicentricity as variables.

Tumour size determined by CESM was correlated with postoperative pathological findings. In addition, age, body mass index (BMI), breast size (self-reported bra cup size), breast density, tumour histology, oestrogen receptor (ER), and progesterone receptor (PR) status, HER-2/neu status, tumour grade, and nodal involvement were also recorded and considered in evaluating the efficacy of CESM in predicting tumour size. The influence of CESM descriptors on the precision of tumour sizing, as previously categorized,[19,20] were also studied.

CESM and image analysis

For CESM, it is necessary to have an automatic contrast medium injection pump, one digital mammography kit equipped with a breast compression system with aluminium or copper filters, and a working station equipped with the application Senobright® (General Electric Healthcare, Buckinghamshire, UK). The CESM procedure was performed as described previously.[11,21,22] Briefly, with the patient in the seated position iodinated contrast medium was administered (1.5 mg/kg iv, at 3 ml/s), and after 2 minutes, the acquisition of low-energy (28 kVp) and high-energy (47 kVp) images began in the following order[1]: medial–lateral oblique view, non-suspicious breast[2]; cranial–caudal view, non-suspicious breast[3]; cranial–caudal view, suspicious breast; and[4] medial–lateral oblique view, suspicious breast, with a total time for the acquisition of all images of 5 minutes (Fig 1).

For the interobserver agreement study, image analysis was performed independently by four certified radiologists with at least 2 years of experience using CESM. Radiologists were provided with a list of previously selected patients by another certified radiologist, who was not involved in image

Please cite this article in press as: Travieso-Aja M. del Mar, et al., Factors affecting the precision of lesion sizing with contrast-enhanced spectral mammography, Clinical Radiology (2017), https://doi.org/10.1016/j.crad.2017.10.017