

SHORT REPORT

THE TUMOUR BORDER ON CONTRAST-ENHANCED SPECTRAL MAMMOGRAPHY AND ITS RELATION TO HISTOLOGICAL CHARACTERISTICS OF INVASIVE BREAST CANCER

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Contrast-enhanced spectral mammography (CESM) is one of the new diagnostic modalities implemented in clinical practice. In the case of these techniques, there are two major issues to be addressed: (1) their diagnostic usefulness, and (2) the relation between parameters assessed using these techniques and well-known diagnostic/prognostic/predictive markers (histological, clinical, and molecular). Therefore, we studied the relationship between the tumour margin assessed on CESM and (1) tumour borders defined on the basis of macroscopic and microscopic examination, (2) pT, (3) pN, and (4) tumour grade in a group of 82 breast cancer patients.

Based on CESM, the tumour border was defined as sharp, indistinct or spiculated, whereas in the case of lesions showing weak or medium enhancement on CESM the borders were classified as unspecified.

We found a statistically significant relationship between tumour margin on CESM and (1) macroscopic border (a spiculated margin on CESM was found only in carcinomas with an invasive border on histological examination; $p = 0.004$), (2) pT ($p = 0.016$), and (3) pN (nodal involvement was observed most frequently in carcinomas with a spiculated or indistinct margin on CESM; $p = 0.045$). Moreover, in cases with an undefined margin on CESM (cases showing weak or medium enhancement on CESM), both invasive and pushing borders were found on histological examination.

The results of our preliminary study suggest that it is possible to assess macroscopic borders of examined lesions on the basis of CESM imaging. This might be useful in planning the extent of surgical excision. On the other hand, the assessment of the tumour margin on CESM might not be precise in cases showing weak enhancement.

Key words: contrast-enhanced spectral mammography (CESM), tumour margin on CESM, macroscopic and microscopic borders.

Introduction

Sensitivity of mammography (MG), which is the primary method in breast cancer diagnostics, ranges from 63 to 98%; however, in dense glandular breasts it is lower, within the range of 30–48%. Therefore, there is an urgent need for development of new diagnostic methods. One such method is contrast-enhanced spectral mammography (CESM), in which images are taken after intravenous contrast administration [1, 2, 3].

Regarding new imaging techniques, there are two major issues to be addressed: their diagnostic usefulness, and the relation between parameters assessed using these techniques and well-known diagnostic/prognostic/predictive markers (histological, clinical, and molecular). In other words, it is postulated that radiological images may carry information about lesion pathophysiology [4, 5].

One of the parameters assessed with all imaging modalities (MG, contrast-enhanced magnetic resonance imaging [MRI], and CESM) is the lesion border/margin, which could be described as sharp, indistinct, or spiculated [6]. Until now the relation between the lesion border assessed using CESM and macroscopic/microscopic borders of breast cancer has not been described in the literature. Therefore, we studied the relationship between tumour margin on CESM and (1) tumour borders defined on the basis of macroscopic and microscopic examination, (2) pT, (3) pN, and (4) tumour grade in a group of 82 breast cancer patients.

Material and methods

Patients

For the purpose of this study we retrospectively included 82 breast cancer patients (with 92 lesions) for whom CESM was applied because of glandular breast structure (reported in the previously performed mammography) or for diagnostic purposes (in the case of lesions requiring further diagnostic procedures). Patients with lesions enhancing on CESM were subjected to ultrasonography- or mammography-guided core biopsy or vacuum-assisted core biopsy. Material obtained during biopsies was histologically verified. All patients with breast cancer received radical local therapy (surgery and radiotherapy) followed by hormonal therapy (in the case of steroid receptor-positive carcinomas) and/or systemic therapy (as individually indicated). All diagnostic procedures and treatment were carried out at the diagnostic and clinical departments of Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Cracow Branch. Mean age of patients was 57.0 ± 1.2 (SE) years (range: 27–83 years).

This study was performed in compliance with the Declaration of Helsinki, and it received the approv-

al of the Ethical Committee at the Regional Medical Chamber in Krakow.

Methodology

Contrast-enhanced spectral mammography

In the contrast-enhanced spectral mammography procedure, which is digital mammography, the first image was taken 2 min after the injection of the iodinated contrast agent (the examination began with the healthy breast, with no suspicious lesions). Sequentially, images were taken in the mediolateral oblique view (MLO) and craniocaudal view (CC). At each projection images were obtained at low and high energy. Using CESM, two mammographic images can be compared: a low-energy image that looks like a standard mammogram and a subtraction image that shows contrast-enhanced areas helpful in locating lesions.

For the purpose of the present study – based on CESM, according to the BIRADS classification for MRI adapted for CESM [6] – the lesion margin was defined as sharp, indistinct, or spiculated. Other parameters – lesion localization, the degree of enhancement (none, weak, medium, strong) and enhancement pattern – were also assessed but not included in the statistical analysis. In cases showing weak or medium enhancement on CESM the lesion border was classified as undefined.

Histological examination

Macroscopic description of tumour borders, pT, pN, and tumour grade were retrieved from histopathological reports, while microscopic borders were reassessed for the purpose of the study.

Statistical analysis

The STATISTICA v.12 software (StatSoft, Inc. Tulsa, OK, USA) was used for all calculations. P values < 0.05 were considered significant. The χ^2 test for independence (Pearson's or maximum likelihood) was applied for the assessment of independence between categorical variables.

Results

We found a statistically significant relationship between lesion margin on CESM and: (1) macroscopic border (a spiculated margin on CESM was found only in carcinomas with an invasive border on macroscopic examination; $p = 0.004$), (2) pT ($p = 0.016$), and (3) pN (nodal involvement was observed most frequently in carcinomas with a spiculated or indistinct margin on CESM; $p = 0.045$). No statistically significant relation ($p > 0.05$, Table I) was found between lesion margin on CESM and: (i) microscopic border

Table I. Relations between tumour margin on CESM and histological characteristics of invasive breast cancers

PARAMETER	CATEGORY	TUMOUR MARGIN ON CESM					P
		SPICULATED	INDISTINCT	UNDEFINED*	SHARP		
		94	16	31	46	1	
Histological type	ductal (NST)	80	13	27	39	1	
	lobular	8	2	2	4	0	
	papillary	4	0	2	2	0	
	cribriform	1	1	0	0	0	
	mucinous	1	0	0	1	0	0.815
Macroscopic border	invasive	57	13	22	22	0	
	pushing border	10	0	1	8	1	0.004
Microscopic border	microfocal pattern of invasion	56	11	21	23	1	
	pushing border	1	0	0	1	0	0.625
pT	1	64	9	20	35	0	
	≥ 2	27	7	13	6	1	0.016
pN	0	68	10	21	36	1	
	≥ 1	23	6	12	5	0	0.045
Tumour grade	1	16	2	5	9	0	
	2	47	9	16	22	0	
	3	20	4	8	8	0	0.982

*Tumour margin was categorized as undefined if enhancement on CESM was weak or medium, macroscopic border was assessed in 67 carcinomas, microscopic border in 57 cases, pT and pN in 91, G in 83 cases.
 CESM – contrast-enhanced spectral mammography

(although all tumours with a spiculated or indistinct edge/margin on CESM presented a microfocal pattern of invasion), (ii) histological type of tumour, or (iii) tumour grade. Moreover, in cases with an undefined margin on CESM (cases showing weak or medium enhancement on CESM), both invasive and pushing borders on macroscopic examination were found.

Discussion

Based on the following results obtained in the present study – (i) spiculated margins on CESM were found only in carcinomas with invasive border on macroscopic examination, and (ii) all tumours with a spiculated/indistinct margin on CESM presented a microfocal pattern of invasion (this finding was not statistically confirmed, probably because of an insufficient number of studied cases) – we can suggest that a sharp margin on CESM, confirmed by macroscopic examination of tumour borders, does not necessarily reflect pushing borders on microscopic examination. This statement seems to be important in the context of an intraoperative assessment of the radicality of excision and the width of surgical margins.

Interestingly, in cases with an undefined margin on CESM (cases showing weak or medium enhancement on CESM; Table I), both invasive and pushing

borders on macroscopic examination were found, which suggests that only strong enhancement allows for precise definition of tumour borders.

From the clinical point of view, the most important finding obtained in our study is that nodal involvement was observed most frequently in carcinomas with a spiculated or indistinct margin on CESM. This might be considered as a confirmation of the results of studies demonstrating that a spiculated margin on radiological examination suggests the presence of a suspected lesion, while a sharp edge/margin suggests a benign lesion. On the other hand, in invasive breast carcinomas it was found that a spiculated margin (on MG or MR) was characteristic of less aggressive malignancy (of low histological grade, low Ki-67 index [proliferation marker] or luminal A subtype), while a sharp margin was characteristic of high aggressiveness (high histological grade or triple-negative phenotype) [4, 5, 7, 8]. Similarly to Huang *et al.* [9] (who studied dynamic contrast-enhanced MRI features), we did not find a relation between tumour grade and tumour margin on CESM. Going further in our deliberations, based on other authors' results, it was postulated that the presence of a spiculated tumour margin (on classical MG or MRI) might reflect two processes of different clinical significance: (1) peripheral invasion of cancer into benign structures, and (2) fibrous con-

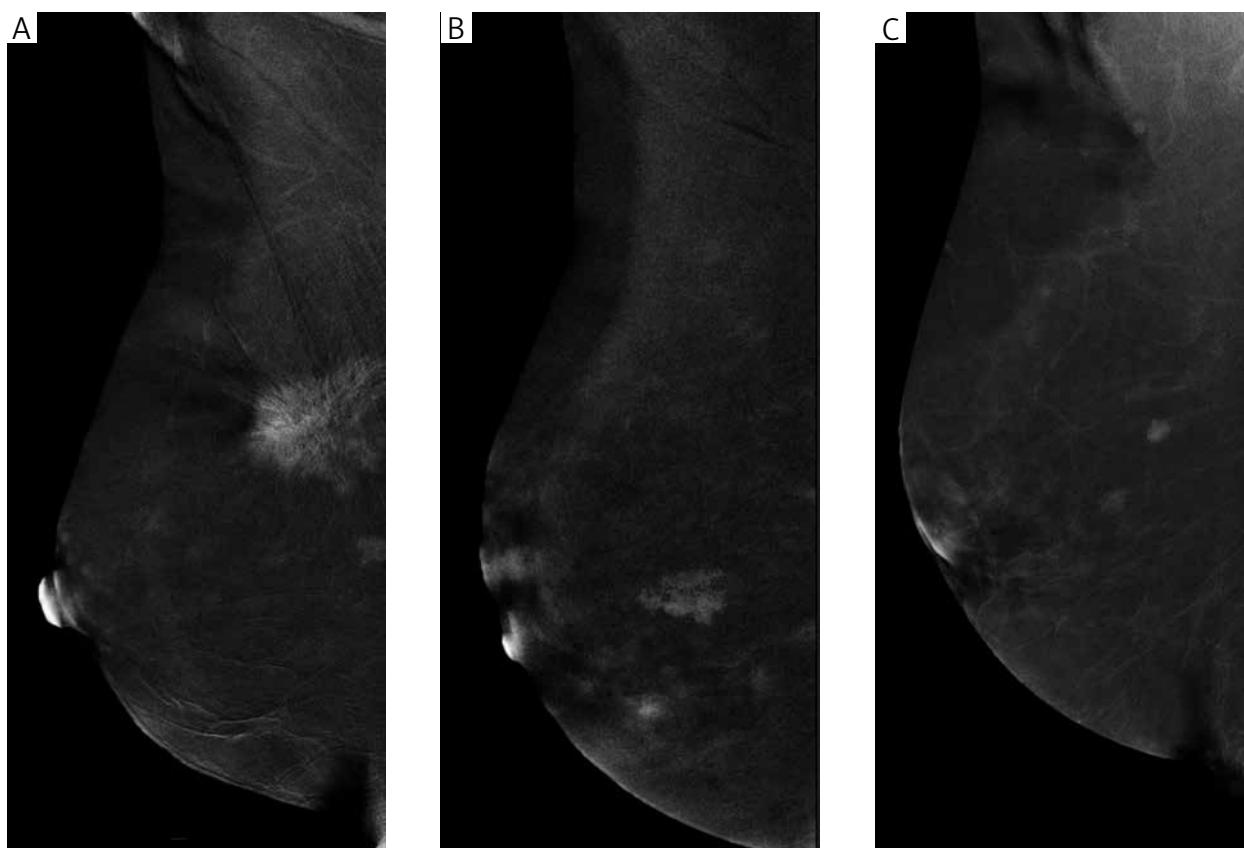


Fig. 1. Tumour border on contrast-enhanced spectral mammography: A) spiculated; B) indistinct, C) sharp. In all cases strong enhancement on CESM was found

nective tissue converging towards malignant cells and limiting their spread [9, 10]. In our opinion, the clinical role of a spiculated margin on CESM might be defined after the analysis of its prognostic significance (such analysis is being planned for the future).

Recapitulating, because of differences in mechanisms of lesion visualization with MG and CESM, there is a need for the assessment of the correlation between CESM characteristics (lesion margin, the degree and pattern of enhancement) and histological/biological/molecular tumour features. We plan to enlarge the studied group and include molecular and/or histological parameters (e.g. vascular density [11]) in order to explain the basis of the radiological tumour picture.

Conclusions

The results of our preliminary study suggest that it is possible to assess macroscopic borders of examined lesions on the basis of CESM imaging. This might be useful in planning the extent of surgical excision. Moreover, the assessment of the tumour margin on CESM might not be precise in cases showing weak enhancement.

The authors declare no conflict of interest.

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