Letter to the Editor

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RE: Is There a Correlation between the Presence of a Spiculated Mass on Mammogram and Luminal A Subtype Breast Cancer?

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Dear Editor:

We read with interest the article "Is there a correlation between the presence of a spiculated mass on mammogram and luminal A subtype breast cancer?" by Liu et al. (1), 2016. We would like to contribute by commenting on the value of mammographic calcification in the presence of a spiculated mass of luminal A molecular subtype.

Mammographic calcification is considered as a major assessment criterion for breast cancer (2). The authors concluded that (1) luminal A subtype of invasive breast cancer was associated with a higher incidence of spiculated mass on a mammogram. We conducted a detailed image analysis (3) of luminal A subtype of invasive breast cancer cases that were admitted to our hospital between 2011 and 2016. We identified 93 cases of the luminal A (spiculated masses vs. non-spiculated masses: 64.5% vs. 35.5%) subtype. This result was consistent with the work reported by Liu et al. (1).

In univariate analysis, calcification morphology (pleomorphic, fine linear, branching, or combined vs. amorphous, or coarse heterogenous odds ratio [OR]: 6.1, $p < 0.05$) and calcification distribution (clustered, grouped, or regional vs. segmental, or linear OR: 5.26, $p < 0.05$) was significantly associated with the presence of a spiculated mass. Using the enter selection, relevant variables with mammographic features of calcifications were selected as predictive factors of the presence of a spiculated mass on a mammogram. In addition, multivariate analysis showed that calcification distribution (clustered, grouped, or regional vs. segmental or linear OR: 6.901, $p < 0.05$) was an independent factor associated with the presence of a spiculated mass of luminal A molecular subtype. The area under the receiver-operating characteristic curve for predicting the presence of a spiculated mass was 0.652. Therefore, we suggest that the future research might be improved by using quantitative methods for assessing the patterns of mammographically detected calcifications.

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Response

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Dear Sir,

We are very glad to receive your letter, and would like to thank you for peer-reviewing our study. Our study indicates a correlation between mammographic spiculation and the luminal A subtype of invasive breast cancer (IBC) (1), which is possibly mediated by the interaction between low histologic-grade tumor cells and adjacent stroma (2). Our results strongly suggest that spiculation is a landmark for IBC wherein tumor cells that have infiltrated through the intact layer of the basement membrane reach the stroma. Clinical observational studies have further corroborated the hypothesis that ductal carcinoma *in situ* is a precursor of IBC. Therefore, we hypothesize that necrotic calcification is a characteristic feature of breast cancer *in situ* stage, as a result of high proliferative activity and disproportionately low blood supply (3, 4). Moreover, necrotic calcification would not occur in the invasive stage since the blood supply is already well established; instead, the emerged calcification in invasive ductal carcinoma is generated prior to the infiltration of tumor cells through the basement membrane and the increase in tumor angiogenesis. Evaluation of calcification in breast lesions is a major assessment criterion for mammographic images. Numerous previous studies have shown a good correlation between breast cancer-associated calcification and subsequent histologic and subtype characteristics (5, 6). However, some concepts and action mechanisms that are necessary for detailed analysis of the mammographic features of breast cancer remain unclear. We agree with the opinion expressed by our peers that future research might be improved by using quantitative methods for assessing the patterns of mammographic features. In the case of calcification, present research is limited by morphological descriptors that are restricted to the global appearance of microcalcification clusters, since the microstructure remains unresolved with the clinical mammography systems in current use (7). Though some imaging modalities could partially solve this problem, they have not yet been applied to clinical practice (8-10). In the past decade, the development of medical-image analysis and recognition tools has facilitated the conversion of images into mineable data and its subsequent analysis for decision support. This practice is termed radiomics (11). In contrast to the traditional practice of treating medical images as pictures intended solely for visual interpretation, radiomic data could be combined with statistics, patient data, and bioinformatics. Therefore, radiomics appears to offer a nearly limitless supply of imaging biomarkers and allows comprehensive quantification of different subtypes of breast cancer (12).

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