Does Texture Analysis of MR Images of Breast Tumors Help Predict Response to Treatment?[1]

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Neoadjuvant chemotherapy is a well-consolidated and powerful treatment for breast cancer that is increasingly offered to patients with locally advanced breast cancer (1,2). Its use is mainly aimed at locally advanced lesions, with the goal of downstaging and size reduction. In addition, neoadjuvant chemotherapy can decrease the tumor burden and facilitate breast conservation in selected patients, without substantial increases in local recurrence. When effective, it may render resectable lesions that previously could not be treated with conservative surgery. Furthermore, the overall survival and recurrence-free survival rates are the same as those for postoperative chemotherapy, and it has shown some promise as a prognostic marker for patient outcome (3,4). In fact, only a small percentage of patients who achieve pathologic complete response will develop disease recurrence and distant metastasis, including patients with clinical stage IIIB cancer, premenopausal status, and fewer than 10 lymph nodes identified (5).

As observed by Chamming's et al (6) in this issue of *Radiology*, this therapeutic approach has also shown some limitations. Although achievement of pathologic complete response in the breast and axillary nodes is the ideal outcome of neoadjuvant chemotherapy, its efficacy is variable, with response rates between 69% and 100%. In particular, recent studies have suggested that it is the chemosensitivity and responsiveness of the tumor, more than the timing of chemotherapy, that influences overall survival (3). Other factors, including the tumor genetic profile and hormone receptor status, also play an important role. In addition, neoadjuvant chemotherapy, like all chemotherapy treatments, may have toxic side effects, could delay other more effective treatments, and has shown a potential for favoring the development of a tumor microenvironment of metastasis (2). For these reasons, the monitoring of response to neoadjuvant chemotherapy is a relevant topic, especially in the initial phases of treatment. Because genetic characterization of breast lesions is expensive and time consuming, there is increased interest in faster, less-expensive, and less-invasive techniques that may provide a risk stratification with the potential to differentiate between good and bad responders to neoadjuvant chemotherapy.

As clearly stated by Chamming's et al (6), intratumoral heterogeneity is a proven biomarker of poor prognosis, and certain heterogeneity patterns may be associated with cancer genetic profiles. Furthermore, intratumoral heterogeneity can be difficult to quantify with traditional imaging tools, especially when a subjective assessment is required.

Recent years have shown an increase in the popularity of several quantification methods applied to imaging techniques that attempt to solve this problem. Many of these methods fall under the definition of texture analysis (7). In texture analysis, various techniques are used to quantify lesion heterogeneity and irregularity of tissue components, based on statistical and transform-based methods, by evaluating the relationships between voxel intensity values in the image. There are many in-house, free, or commercially available software solutions that may be used to conduct the required postprocessing, such as the one indicated by Chamming's et al in their article.

Chamming's et al chose the histogram analysis technique, which is one of the more straightforward and easily implementable texture analysis methods. This technique has the advantage of requiring less processing time when compared with higher-order

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Conflicts of interest are listed at the end of this article.

See also the article by Chamming's et al in this issue.

texture analysis methods, and the value of its derived parameters has been previously demonstrated (8). A possible limitation is that, contrary to more advanced methods, the histogram-derived parameters include no information on the spatial distribution of the intensity values. This may be a potentially viable avenue for further research in the field that may yield even more accurate quantitative imaging biomarkers.

In particular, Chamming's and colleagues studied tumor heterogeneity of breast cancer at pretreatment magnetic resonance (MR) imaging by extracting several quantitative histogram-based parameters and correlating them with the pathologic response to neoadjuvant chemotherapy and tumor histologic features. Upon completing the univariable analysis, they found no significant association between tumor type or hormonal receptor expression and the evaluated texture analysis parameters. However, they did identify kurtosis as an imaging biomarker that correlates with pathologic complete response. This value represents mathematically the "peakedness" of the histogram of pixel intensity value distribution and, as reported by the authors, it is believed to reflect tissue microstructural organization.

Upon completing multiple logistic regression analysis, including tumor type, grade, triple-negative status, and kurtosis on T2-weighted MR images, the authors found that kurtosis on T2-weighted MR images was independently associated with achievement of pathologic complete response in the non–triple-negative breast cancer population ($P = .033$) but not in the triple-negative breast cancer group or in the entire population. This information is particularly important in the non–triple-negative breast cancer group of patients because the response to neoadjuvant chemotherapy is more variable in this category of patients and the data provided may have important clinical and therapeutic implications.

The results of the study by Chamming's et al are also in agreement with those of previous works on the same topic, showing the role of texture analysis as a powerful tool for predicting the response to neoadjuvant chemotherapy at MR imaging (9) and regarding the influence of tumor subtype on the value of kurtosis for prediction of pathologic complete response (10). However, compared with previous works, the article by Chamming's et al showed in a larger number of patients that texture analysis at the pretherapeutic work-up of patients with breast carcinoma is associated with achievement of pathologic complete response.

Another important message of this study is that the results were obtained from an imaging data set acquired during daily clinical practice, with use of commercially available software. These study characteristics indicate that the findings, if further validated with larger studies, could be easily integrated into a clinical diagnostic workflow. Furthermore, whereas most studies on the same topic investigated texture features with postcontrast T1-weighted MR imaging, Chamming's et al also evaluated T2-weighted sequences, which provided good results regarding association with pathologic complete response after neoadjuvant chemotherapy and triple-negative breast cancer status. These findings are especially relevant in light of recent concerns over the use of gadolinium-based contrast agents in MR imaging (11).

Finally, an additional strength of this study is that the authors included in their population only consecutive patients with various pathologic types of breast cancers manifesting as both mass and nonmass lesions at MR imaging.

As pointed out by Chamming's et al, possible limitations of this study include the reproducibility of the method as one of the key issues preventing the widespread use of quantitative markers. They also correctly identified the need to validate findings across different institutions with MR imaging units from different vendors and of field strengths. Still, quantitative imaging is a field that has rightly received growing attention as the technology is improving, and there is a growing awareness for the possibilities of more personalized treatments—especially in the oncologic field. Other limitations include the retrospective data collection and the use of a single institution without any patient randomization. Therefore, a randomized multicenter study in a larger patient population is necessary and could be the next step to validate the findings of this innovative article.

In conclusion, the work by Chamming's et al shows that histogram-derived texture analysis may be easily integrated into the imaging work-up of patients with breast cancer. These parameters, and kurtosis in particular, may be useful for identifying patients with non–triple-negative breast cancer who will show a complete pathologic response to neoadjuvant chemotherapy. Thus, their report further supports the growing concept that quantitative imaging biomarkers may be a less-invasive method of obtaining an earlier prognostic stratification of patients with breast cancer before and during therapy.

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References

1. Ikeda T, Jinno H, Matsu A, Masamura S, Kitajima M. The role of neoadjuvant chemotherapy for breast cancer treatment. Breast Cancer 2002;9(1):8–14.
2. Dave RV, Millican-Slater R, Dodwell D, Horgan K, Sharma N. Neoadjuvant chemotherapy with MRI monitoring for breast cancer. Br J Surg 2017;104(9):1177–1187.
3. Teshome M, Hunt KK. Neoadjuvant therapy in the treatment of breast cancer. Surg Oncol Clin N Am 2014;23(3):505–523.
4. Karagiannis GS, Pastoriza JM, Wang Y, et al. Neoadjuvant chemotherapy induces breast cancer metastasis through a TMEM-mediated mechanism. Sci Transl Med 2017;9(397):eaan0026.
5. Gonzalez-Angulo AM, McGuire SE, Buchholz TA, et al. Factors predictive of distant metastases in patients with breast cancer who have a pathologic complete response after neoadjuvant chemotherapy. J Clin Oncol 2005;23(28):7098–7104.
6. Chamming's F, Ueno Y, Ferré R, et al. Features from computerized texture analysis of breast cancers at pretreatment MR imaging are associated with response to neoadjuvant

chemotherapy. Radiology 2018;286(2):412–420.

7. Lubner MG, Smith AD, Sandrasegaran K, Sahani DV, Pickhardt PJ. CT texture analysis: definitions, applications, biologic correlates, and challenges. RadioGraphics 2017;37(5):1483–1503.

8. Just N. Improving tumour heterogeneity MRI assessment with histograms. Br J Cancer 2014;111(12):2205–2213.

9. Ahmed A, Gibbs P, Pickles M, Turnbull L. Texture analysis in assessment and prediction of chemotherapy response in breast cancer. J Magn Reson Imaging 2013;38(1):89–101.

10. Drisis S, Metens T, Ignatiadis M, Stathopoulos K, Chao SL, Lemort M. Quantitative DCE-MRI for prediction of pathological complete response following neoadjuvant treatment for locally advanced breast cancer: the impact of breast cancer subtypes on the diagnostic accuracy. Eur Radiol 2016;26(5):1474–1484.

11. Gulani V, Calamante F, Shellock FG, et al. Gadolinium deposition in the brain: summary of evidence and recommendations. Lancet Neurol 2017;16(7):564–570.