

The Feasibility of utilizing Vascularity Characteristics in Three-Dimensional Power Doppler Ultrasonography to Predict Complete Responses in Patients Undergoing Neoadjuvant Chemotherapy

Wei-Chung Shia¹ PhD, Dar-Ren Chen^{1,2*} MD, Yu-Len Huang² PhD, and Hwa-Koon Wu⁴ MD and Fang-Rong Hsu⁵

¹Cancer Research Center, Changhua Christian Hospital, Taiwan

²Comprehensive Breast Cancer Center, Changhua Christian Hospital, Taiwan

³Department of Computer Science, Tunghai University, Taiwan

⁴Department of Medical Imaging, Changhua Christian Hospital, Taiwan

⁵Department of Information Engineering and Computer Science, Feng Chia University, Taiwan

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***Corresponding author:** Dar-Ren Chen, Comprehensive Breast Cancer Center, Changhua Christian Hospital, 135 Nanhsiao Street, Changhua City 50006, Taiwan, Tel: +886-4-723-8595; Fax: +886-4-722-8289; Email: darren_chen@cch.org.tw

Abstract

Pathological complete response (pCR) is most significantly associated with the likelihood of benefit in neoadjuvant chemotherapy (NAC) treatment. Tumor vascularity and morphology is shown has correlated with the degree of malignancy and prognosis, therefore the change of the vascularity and morphology may help predict the pCR of neoadjuvant chemotherapy for breast cancer. Two new studies which published recently represent that utilized the 3D-HDF ultrasound (US) to quantify vascularity characteristics and identify differences associated with varying levels of chemotherapeutic response is possible.

Keywords: Neoadjuvant chemotherapy, 3D-HDF ultrasound, Breast cancer, Pathological complete response

Introduction

To increase the chances of successful breast-conserving surgery, neoadjuvant chemotherapy is aimed at reducing the tumor size and stage [1]. Pathological complete response (pCR) is most significantly associated with the likelihood of benefit, as measured by disease-free and overall survival together with the lymph node status at surgery [2]. In the past studies, tumor vascularity and morphology has shown the strongly correlated with the degree of malignancy [3,4] and prognosis [5]; therefore, changes in this vascularity and morphology may predict pCR to neoadjuvant chemotherapy for breast cancer. The challenge is how to classify patients with a good and poor response after treatment based on the changes in vascular flow indices. Predicting which patients will experience pCR will help identify patients who are likely to benefit from treatment.

Two new studies which published recently represent that utilized the 3D-HDF US to quantify vascularity characteristics and identify differences associated with varying levels of

chemotherapeutic response is possible [6,7]. These studies were focus to patients were stage T2 (tumor size 2 cm to 5 cm) under the estimate within tumor, node and metastasis (TNM) staging system according to the 6th AJCC [8], and receiving anthracycline-based therapies (FEC). These studies results show that the vascularity variations within sonography was provide sufficient information to directly improve the observation of the chemotherapy response.

If the analysis was simply based on the variation of fundamental vascular flow indices, over 83% of pCR patients (AUC \approx 0.7) can be distinguished before the initiation of chemotherapy approximately. Over 87% of pCR patients can be distinguished before the third cycle of chemotherapy approximately (AUC \approx from 0.75 to 0.82). After combine the variation of vascular flow indices and morphological features, over 89% of pCR patients can be distinguished before the initiation of chemotherapy (AUC = 0.8788). Over 93% of pCR patients was observed before the

2nd cycle of chemotherapy (AUC = 0.8551). After the analysis, the trend of flow index (FI) in the vascular flow indices of sonography is valuable information to help distinguish between good and poor responders to chemotherapy. The variation in FI at each cycle of chemotherapy was different in the poor responder group compared to the pCR and PR groups. It shows the flow characteristics of tumor vascularization can be a key factor for predicting the effects of neoadjuvant chemotherapy.

There are several limitations were present in these studies, include the chemotherapy therapy regimen was focus to the FEC, and fewer HER2-positive patients enrolled of case group. The smaller sample size also cannot comprehensively include all combinations of ER/PR/HER2 expression status in breast cancer patients. To compare the vascularity and morphology difference of patients between FEC or other regimens, the imaging data from five CR (complete response) patients who were treated with TCH (docetaxel + cyclophosphamide + trastuzumab) were collected to compare the trends of VI/FI/VFI between taxane-based to FEC regimen. The curve of VI/FI/VFI of CR patients who administrated with TCH were represent the trends is very similar to the CR patients who administrated with ECT. This preliminary evidence that may conclusion of this study is also applicable to taxane-based regimens. After improved the size of case group to 76 patients (include 41 pCR patients and 16 HER2-positive patients), over 75% of the pCR patients were distinguished before the first chemotherapy administration (AUC = 0.8247, Accuracy = 75.61%).

Conclusion

Even the acquisition of a sonography is dependent on highly-experienced expert and is associated with several unavoidable biases, the variations of vascularity in sonography on lesion still shows it can aid in the evaluation of the chemotherapy response in breast cancer. The preliminary result of recent studies and

the extended test has already represented the potential of using the vascularity information of sonography as the characteristic and predict the response of NAC. After obtain the larger dataset in the future, how to make the model optimizes and having the good performance in distinguish pCR patients becomes the new challenge, and the feasibility and how to aid the decision-making of physicians in NAC will be reveal finally.

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