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Research Article

Evaluating the Role of Computed Tomography in the Assessment of Breast Tumour Response to Chemotherapy

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2. Key words

Computed tomography, Radiological response, Complete pathological response

1. Abstract

Background. Breast magnetic resonance imaging (MRI) is currently the most accurate indicator of the response to pre-operative chemotherapy but is seldom used because of its cost. Contrast enhanced computed tomography (CT) is often done for re-staging prior to surgery and we hypothesise that enhancement, or the lack of it, can indicate tumor viability. Aims. We examined the correlation between radiological response on CT and actual pathological response, specifically whether CT predicted for complete pathological response (pCR). Methods. Retrospective evaluation was performed of 141 women (total of 145 tumors) who had undergone surgery after pre-operative chemotherapy. Radiological response (comparison of the pre- and post-chemotherapy CTs) was correlated with pathological response and potential predictors of response were examined. Results. CT had a sensitivity of 40.9% and specificity of 85.4% in predicting pCR. There was a significant correlation between radiological and pathological response (P = 0.002), but only a third of those with complete radiological response (rCR) had pCR. Women with smaller tumors (P = 0.001) and who had completed the systemic treatment schedule (P = 0.014) were more often found with rCR. There was no significant correlation between pCR and the resolution of enhancement (P = 0.128), although half the tumors with no residual enhancement had pCR compared to none of the tumors with a significant degree of residual enhancement. Conclusion. Residual tumor on CT often indicates the presence of residual disease. However, two-thirds of cases with rCR still had residual disease at surgery, implying that CT therefore cannot reliably predict pCR.

3. Introduction

Surgery may be of little benefit when there is complete pathological response (pCR) after neoadjuvant chemotherapy. However, omitting locoregional treatment would be possible only if pCR can be accurately predicted. Current modalities have limited accuracy in predicting pCR [1,2] and consequently, it remains the standard of care to resect the breast or at least the original tumour bed after neoadjuvant chemotherapy in order to determine the pathological response, regardless of the clinical or radiological response.

Previously at our unit, neoadjuvant chemotherapy was given mostly to downstage locally advanced tumours to facilitate surgery. Downsizing to facilitate breast conservation was rarely done and many women would opt for surgery upfront, perceiving it to be more effective than chemotherapy. Since survival outcomes were thought to be equivalent whether chemotherapy was given in the neoadjuvant or adjuvant setting,[3] there seemed little need to actively push for neoadjuvant chemotherapy when there was a clear patient preference for surgery upfront. However, emerging evidence of a survival benefit in women with oestrogen receptor (ER)-negative human epidermal growth factor receptor (HER)-2-positive tumours, and likely also in triple negative cancers, has led to a stronger push for neoadjuvant chemotherapy in these tumour subtypes, even for smaller node-negative tumours [4,5]. The high pCR rates now being achieved, especially with dual anti-HER2 blockade, have renewed interest in selecting only those with residual disease for surgery [6]. Biopsy of the original tumour bed is being explored as a surrogate predictor of response, whereby a negative biopsy would mean pCR and could consequently mean that surgery may be omitted [7]. Many studies select women with complete or near complete radiological response for biopsy, thereby making the accuracy of the imaging modality crucial. Breast magnetic resonance imaging (MRI) is currently considered the superior modality for the assessment of tumour response post-neoadjuvant chemotherapy, although it too has its limitations [8,9]. One of the main advantages of MRI is the use of dynamic contrast enhanced sequences,

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where enhancement results from the increased neo-angiogenesis and microvascular permeability commonly encountered in actively growing tumours. Conversely, a reduction in enhancement then implies reduced tumour activity in response to treatment and the absence of enhancement in a residual mass can indicate necrotic non-viable tumour [10].

Breast MRI is not often done at our unit primarily because of its high cost and also because it does not change management in many of our women who tend to opt for mastectomy over breast conservation [11]. On the other hand, a post-treatment contrast enhanced computed tomography (CT) scan is often done prior to surgery to reassess local disease extent and to exclude metastatic progression, since many of the women receiving neoadjuvant chemotherapy have locally advanced disease. Since CT also includes contrast enhanced sequences, we hypothesised that it could also indicate tumour response to treatment and we sought to determine how well radiological response on CT correlated with the actual pathological response and to identify predictors of response. We also evaluated breast ultrasound in the subgroup of women who also received it post-treatment.

4. Methodology

Women diagnosed with invasive breast cancer who had received primary chemotherapy from between January 2007 to December 2019 were included in the study if pre- and post-treatment CT assessments had been performed. These women were identified from our prospective breast cancer database. This study has ethics committee approval (2019/00217). Women were included regardless of whether chemotherapy had been given with curative or palliative intent, so long as they subsequently underwent surgery and the pathological response was known. All chemotherapy and targeted therapy regimens were included, and women were also included regardless of whether they had completed the scheduled regimen. Some women also underwent post-treatment mammogram and breast ultrasound assessments, and a few underwent breast MRI; these were also reviewed. Typically, a woman would undergo diagnostic mammogram and breast ultrasound followed by a biopsy for histological confirmation of breast cancer. Primary chemotherapy would be recommended in women with metastatic disease at presentation while the decision for neoadjuvant chemotherapy for potentially curative disease would be made following discussion at the multidisciplinary tumour board and with the patient. Staging generally comprised of a CT scan of the thorax, abdomen and pelvis and a bone scan. Unless there were contraindications, such as documented contrast allergy or renal impairment, CT scans would be done with intravenous contrast. Women with HER2-positive disease were offered trastuzumab in combination with chemotherapy, which often comprised of an anthracycline-based regimen and taxanes (4 cycles of doxorubicin / cyclophosphamide and 12 cycles of paclitaxel being the most common, which was also the most commonly administered regimen in women with other tumour subtypes). In more recent years, from 2018 onwards, dual anti-HER2 blockade regimens were increasingly used, such as the TCH / TCHP regimen (Docetaxel / Carboplatin / Herceptin or Perzutumab). Women with metastatic disease received non-anthracycline based regimen, most commonly 12 cycles of paclitaxel. Following completion of the systemic treatment regimen, re-staging with CT scans were done, as well as breast mammogram and ultrasound in some instances. A repeat biopsy was not done, unless in instances where there was suspicion of new disease that would change the surgical management. The women would then proceed with surgery and pathological response would be determined on histological analysis of the surgical specimen.

Contrast enhanced CT scan of the thorax, abdomen and pelvis was performed covering from the lung apex to the iliac crests. The CT studies were performed on a 64-detector CT system (GE Light Speed VCT or GE Discovery CT750 HD, GE Healthcare, Milwaukee, WI). The imaging protocol used the following parameters: section width, 0.625mm; reconstruction interval, 0.625mm; pitch, 0.984; 120kV; and 250mA. All patients received a bolus of 80 to 100mL of intravenous iodinated contrast medium (Omnipaque/ Iohexol 350 mg Iodine/ml; GE Healthcare) at a rate of 3 mL/s with the use of a power injector via an 18 or 20-gauge cannula in an antecubital vein. The scan commenced about 60seconds after the administration of the contrast medium. Images were then reformatted in coronal and sagittal planes. Pre- and post-treatment CT images were compared and treatment response (in the tumour and nodes) was assessed according to the RECIST 1.1 criteria, where the sum of the largest dimension of tumours pre-treatment was compared with its variation post-treatment and response classified as: complete response; partial response (≥ 30% dimensional reduction), stable disease (<30% dimensional reduction or <20% dimensional increase), disease progression (>20% diameter increase or appearance of new lesion).

Full Field Digital Mammogram (FFDM) was performed in every patient for both breasts in standard cranio-caudal and medio-lateral oblique projections at diagnosis. Additional views like magnification views, cone compression views were acquired, when needed. The mammograms were acquired on either Amulet FFDM system (Fujifilm Medical, Tokyo, Japan) or Mammomat Nova 3000 (Siemens AG, Munich, Germany) using automatic exposure control. Breast ultrasound was performed either using Acuson S2000 system (Siemens Medical Solutions, Mountain View, USA) or Toshiba Aplio 80 (Toshiba Inc., Tokyo, Japan). Both machines were equipped with a variable-frequency linear array transducer set at 9–14 MHz. The ultrasound was performed in supine position with arm above head while scanning. The breast tumor was assessed for location, distance from nipple, size, morphology and internal vascularity. Axillary nodes were also assessed for abnor-

mal morphology. Pre- and post-treatment images were compared, and response was assessed according to the RECIST 1.1 criteria as described earlier.

Radiological complete response (rCR) was defined as the complete regression of the previously documented cancer and/or abnormal regional nodes. Regional nodes that were still detected on imaging, but which were considered to be of normal morphology or within the normal size criteria were considered normal. New additional lesions on the post-treatment scans were defined as lesions that were deemed suspicious or indeterminate for new disease (satellite lesions), but which were not seen on the previous imaging done pre-treatment. In addition, we separately evaluated the significance of enhancement on CT; tumours that were still detected on the post-treatment CT were stratified according to whether there was persistent enhancement, only minimal residual enhancement, or no more residual enhancement.

True positives (TP) are defined as the number of cases where tumours showing radiological complete response (rCR) were also found to have complete pathological response (pCR) at surgery. True negatives (TN) are defined as cases where tumours showing residual diseae on imaging were also found to have residual disease at surgery (no pCR). False positives (FP) was defined as the number of cases where tumours showing rCR are found with residual tumour at surgery. False negatives (FN) were defined as the number of cases where tumours showing residual disease on imaging were found in fact to have pCR at surgery. Sensitivity was defined as the probability of pCR being detected on imaging and was calculated by TP/(TP + FN). Specificity was defined as the probability of residual disease at surgery (no pCR) being detected on imaging and was calculated by TN/(TN + FP). Positive predictive value was defined as the probability by which pCR was predicted by rCR (TP/(TP + FP) and negative predictive value was defined as the probability by which residual disease documented on imaging (no rCR) predicted for residual disease at surgery (no pCR) (TN/(TN + FN). The association between the radiological and pathological response, and the association of radiological response with standard clinical pathological parameters available pre-operatively were evaluated with univariate analyses (Chi-square test, Fisher's test where appropriate) and were performed using GraphPad Prism version 6 (GraphPad Software, San Diego, United States). A 2-tailed P value test was used for all analyses, and a value of $P < 0.05$ was considered statistically significant.

5. Results

5.1. Patient Demographics

The study included 141 women who had received primary chemotherapy. Of these, 15 women had metastatic disease at presentation and chemotherapy was palliative in intent. There was a total of 145 tumors; 4 of the women had bilateral invasive cancer. Median age at diagnosis was 56 years (ranging from 32 to 80 years); 94 women were of Chinese ethnicity, 21 women were of Malay ethnicity, 5 women were of Indian ethnicity and the rest belonged to other ethnicities. Disease was staged as Stage II in 28 women, as Stage III in 98 women and as Stage IV in 15 women. Fifty-six women had multifocal disease on the initial work up and 111 women had nodal involvement. The majority of tumors (133 of 145) were classified as invasive ductal carcinoma not otherwise specified, 3 as invasive lobular carcinoma, 5 as invasive mucinous carcioma, 1 as invasive metaplastic carcinoma. Three tumours were reported only as invasive carcinoma at biopsy, with no morphology details; no residual tumour was found at surgery in 1 and only residual DCIS was present in the other 2.

Thirty tumors (occurring in 30 women) were triple negative (negative for ER, progesterone receptor (PR) and HER2 receptor expression). All 30 women, except 2 women, received anthracycline-based chemotherapy; 1 woman with metastatic disease received 12 cycles of paclitaxel and the other woman received 4 cycles of carboplatin. A total of 58 tumors (occurring in 58 women) were HER2-positive (33 were also ER-negative and 25 were ER-positive). Three women had refused anti-HER2 treatment although they received and completed anthracycline-based chemotherapy. Forty-eight women received trastuzumab: 34 in combination with an anthracycline-based chemotherapy regimen and the rest in combination with a taxane. Another 7 women received dual anti-HER2 blockade (trastuzumab and perzutumab); 3 as the TCHP regimen, 3 in combination with paclitaxel sequential to doxorubicin/cyclophosphamide and 1 following doxorubicin/cyclophosphamide alone. Overall, 22 women did not complete the systemic treatment schedule, but only 4 women received less than 50% of the treatment dose. Complete pathological response (pCR) was documented in 22 of 145 tumors (15.2%).

5.2. Correlation of CT Response with Pathological Response

Radiological complete response (rCR) on CT was documented in 27 of 145 (18.6%) cases. All these 27 tumors occurred in women who had completed the scheduled systemic therapy, with all except one, completing an anthracycline-based regimen. The last woman completed 12 cycles of paclitaxel and achieved pCR. Two of 13 women with HER2-positive tumors received dual anti-HER2 blockade, while the rest received trastuzumab alone.

Complete pathological response was documented at surgery in 9 of 27 cases of rCR, giving CT a positive predictive value of 33.3% (Table 1). On the other hand, negative predictive value was 89.0% and residual disease was likely to be present (no pCR) in absence of rCR on CT. No residual disease (pCR) was found in 13 instances despite a residual tumor mass still being present on post-treatment CT; 10 of which were non-enhancing and 3 of which showed only minimal enhancement confined to the tumor edges. Seven of these

13 cases also showed complete regression of abnormal nodes on the post-treatment CT. Overall, CT scans had a sensitivity of 40.9% and specificity of 85.4% in predicting pCR (Table 1). Complete radiological response (rCR) correlated strongly with pCR (P = 0.002, OR 5.400, 95% CI 1.928 to 15.12) (Table 2) and occurred more frequently in smaller tumors and in women who completed the planned systemic treatment regimen (P = 0.001, OR 4.006, 95% CI 1.670 to 9.608 and P = 0.014, OR 12.82, 95% CI 0.753 to 218.4 respectively). The association with tumor subtype was not statistically significant (P = 0.502), although 30% of triple negative tumors and 22.4% of HER2-positive tumors achieved rCR compared to only 14.0% of ER-positive/HER2-negative tumors. We did not identify any factors that were associated with a discordant finding of rCR and pCR (Table 3).

Table 1: Tabulation of numbers (percentage of the entire cohort) for radiological response on CT assessment with respect to pathological response (n = 145).

	Complete pathological response (pCR)	Residual disease (no pCR)
Complete radiological response (rCR)	9 (6.2)	18 (12.4)
Residual disease on CT	13 (9.0)	105 (72.4)

Table 2: Univariate correlation analyses between radiological response and clinicopathological factors available at the time of biopsy (n = 145). rCR: complete radiological response on CT; TNBC: triple negative breast cancer; HER2: human epidermal growth factor receptor-2; pCR: complete pathological response. T1: tumours up to 2cm, T2: tumours up to 5cm, T3 tumours more than 5cm, T4: tumours of any size with skin or chest wall involvement.

	Radiological Complete Response (rCR) (n = 27)	Residual disease on CT (n = 118)	P value
T stage at diagnosis			
T1 and T2	14	25	0.001
T3 and T4	13	93	
Nodal involvement at diagnosis			
Positive	22	106	0.224
Negative	5	12	
Metastasis at presentation			
No	26	105	0.468
Yes	1	13	
Tumour subtype			
TNBC	6	24	0.502
HER2-positive	13	45	
ER-positive / HER2-negative	8	49	
Primary systemic therapy			
Completed	27	96	0.014
Not completed	0	22	
Pathological response			
pCR	9	10	0.002
Residual disease	18	108	

Table 3: Univariate correlation analyses between complete radiological and pathological response with clinicopathological factors available at the time of biopsy (n = 27). rCR: complete radiological response (on CT); pCR: complete pathological response; ER: oestrogen receptor; HER2: human epidermal growth factor receptor-2.

	rCR and pCR (n = 9)	rCR but no pCR (n = 18)	P value
Median Age (years)	48 (40 to 80)	52 (33 to 75)	0.701
T stage at diagnosis			
T1 and T2	5	9	1.000
T3 and T4	4	9	
Nodal involvement at diagnosis			
Positive	8	14	0.636
Negative	1	4	
Tumour histology			
Invasive ductal carcinoma	9	17	1.000
Invasive lobular carcinoma	0	1	
ER status			
Positive	4	8	1.000
Negative	5	10	
HER2 status			
Positive	6	7	0.237
Negative	3	11	

5.3. CT Assessment of Tumor Response

A total of 36 tumors showed complete regression on CT and another 97 tumors showed partial response, of which 19 no longer enhanced. Six tumors were stable and 4 had progressed. A mixed response was noted in 2 cases, both showed complete response in one tumor but partial response in a second tumor foci. A reduction in enhancement was observed in all tumors following treatment, with residual enhancement being present in 88 tumors. We did not observe a statistically significant association between the resolution of enhancement and pCR (P = 0.128). However, the frequency of pCR seemed associated with the degree of residual enhancement; pCR was noted in 10 of 19 tumors with complete resolution of enhancement, in 3 of 21 tumors with only minimal enhancement, while none of the 67 tumors with a significant degree of enhancement had pCR. Given that pCR was common in instances where the residual tumor no longer enhanced on CT, we combined such cases with cases of rCR and found CT to have a sensitivity of 86.4% and specificity of 69.1% in predicting for pCR (Table 4). However, the positive predictive value remained low at 33.3%, with residual disease being found at surgery in 38 of 57 instances. Despite the complete regression of enhancement, residual disease was present in 11 of 21 non-enhancing tumors, 2 with residual DCIS and 19 with residual invasive carcinoma ranging in extent from 1 to 100mm. Negative predictive value was 96.6%. The 3 cases of pCR without rCR, the residual mass showed significant reduction in size and only minimal residual enhancement was present.

Table 4: Tabulation of numbers (percentage of the entire cohort) for radiological response on CT assessment with respect to pathological response (n = 145).

N = 145	Complete Pathological Response	Residual disease (no pCR)
Complete radiological response on CT Or residual non-enhancing tumour	19 (13.1)	38 (26.2)
Residual tumour with enhancement	3 (2.1)	85 (58.6)

5.4. Ultrasound Assessment of Tumor Response

Post-treatment ultrasound was also performed in 36 patients. Residual disease was reported in 33 cases, including 8 instances where new lesions were also seen. None of these new lesions had corresponding lesions seen on the CT and in fact, rCR on CT was reported in 4 of these 8 cases. Breast MRI was done to further evaluate the new lesions in 2 cases; none of these women had a pre-treatment MRI. In one case where rCR was reported on CT, MRI picked up a mildly enhancing lesion corresponding to the original tumor bed, which was later confirmed to be residual invasive ductal carcinoma at surgery. In the other case, where partial response was reported on CT, MRI detected a 26mm by 11mm area of non-mass enhancement that corresponded to the new lesion seen on ultrasound, which was histologically proven to be DCIS. Only 6 of these 36 tumors with post-treatment ultrasound assessment had pCR at surgery. No residual focal lesion was seen on US in 1 case, while a residual mass, though smaller than before, was still reported in the remaining 5 cases. In 1 of the 5 cases, interval development of new nodules worrisome for satellite lesions adjacent to the main lesion was further reported but these were not found to be new disease at surgery. Ultrasound had a sensitivity of 16.7% and specificity 93.3% in predicting pCR. Positive predictive value was 33.3% and negative predictive value was 84.4% (Table 5).

Table 5: Tabulation of numbers (percentage of the entire cohort) for radiological response on US assessment with respect to pathological response (n = 36).

	Complete pathological response (pCR)	Residual disease (no pCR)
Complete response on US	1 (2.8)	2 (5.6)
Residual and/or new lesions	5 (13.9)	28 (77.8)

5.5. Assessment of Nodal Response

Abnormal nodes suggestive of nodal involvement were reported on the initial pre-treatment CT in 136 tumours. Complete resolution was reported in 55 cases on the post-treatment CT, and 37 of these were found with no residual nodal disease at surgery. Computed tomography prediction of complete nodal response had a sensitivity of 58.2% and specificity of 76.8%. Positive predictive value of CT was 70.1% and negative predictive value was 65.4%. Abnormal nodes were seen on pre-treatment ultrasound in 35 patients (of 36 patients who had post-treatment done). Complete regression of the nodal disease was seen on the post-treatment ultrasound in 15 patients and pCR in the nodes was found in 9. Of 20 patients reported with either partial response or stable disease in the nodes on ultrasound, 7 had no residual nodal disease. The number of involved nodes in those with residual nodal disease ranged from 1 to 8.

5.6. Concordance of Imaging Assessments with Pathological Response

We next evaluated the concordance between post-treatment CT and breast ultrasound in the 36 patients who also had post-treatment ultrasound one. Both assessments were concordant with the pathological response at surgery in 21 patients (58.3%). There was only 1 patient who had rCR on both CT and US who had achieved 3 pCR. Twenty-three patients had residual disease demonstrated on both CT and US and 20 were found with residual tumor at surgery, while the remaining 3 had pCR (Table 6). Assessment of nodal status was concordant with the pathological response in the nodes in 18 patients. Six were reported to have complete regression of nodal disease on both CT and US and were found to have no residual nodal disease at surgery. Twelve others were found with residual nodal disease as predicted by the CT and ultrasound.

Table 6: Tabulation of numbers (percentage) of combined computed tomography (CT) and ultrasound (US) assessment of radiological response stratified by pathological response (n = 36) *1 patients had no abnormal nodes on pre-treatment CT and US.

	Complete pathological response (pCR)	Residual disease (no pCR)
Tumour Assessment		
rCR on both CT and US	1 (2.8)	0
rCR on CT (residual tumour on US)	2 (5.6)	8 (22.2)
rCR on US (residual tumour on CT)	0	2 (5.6)
Residual tumour on both CT and US	3 (8.3)	20 (55.6)
Nodal Assessment*		
rCR on both CT and US	6 (16.7)	3 (8.3)
rCR on CT (residual tumour on US)	4 (11.1)	0
rCR on US (residual tumour on CT)	1 (2.8)	2 (5.6)
Residual tumour on both CT and US	7 (19.4)	12 (33.3)

6. Discussion

The low rate of rCR and pCR in our study can be explained by the high proportion of women with locally advanced disease. Like others, we observed that rCR was more common with smaller tumors. Women presenting to our unit are generally less receptive to neoadjuvant chemotherapy and perceive surgical removal of the tumor to be the more effective and quicker treatment. In the past where it was believed that neoadjuvant chemotherapy did not confer a

survival advantage, there was less impetus to push for neoadjuvant chemotherapy unless upfront surgery was expected to be difficult or extensive. Since such women are at risk of disease progression while on chemotherapy, a post-treatment CT was often done to re-assess disease extent prior to surgery [12].

At present, post-treatment response is assessed primarily by clinical examination, but post-treatment fibrosis is often indistinguishable from viable tumor and complete clinical response correlates poorly with pCR. Mammogram and breast ultrasound are more accurate than clinical assessment but are not often repeated post-treatment largely because most women opt for a mastectomy anyhow [8]. Re-staging CT scans, on the other hand, are more commonly done post-treatment for surgical planning. There have been no studies describing CT assessment of tumor response to chemotherapy. While CT is not a dedicated breast imaging and lacks the resolution of mammogram and ultrasound, it demonstrates enhancement, or the lack of it, which can provide information on tumor viability. Ultrasound outperforms mammography in predicting pathological tumor size after neoadjuvant chemotherapy, [8,13] but it demonstrates only morphological changes and tumor cell death may not manifest as a change in lesion size till much later. Consequently, focal lesions seen on ultrasound may not necessarily represent viable tumor. In our study, a residual tumor mass was still seen on post-treatment ultrasound in 5 of 6 women with pCR, implying that the sonographic lesions were merely fibrosis or necrotic tumor. Changes in lesion size can lag behind cell death, given the time required for tumor cell debri to be cleared by macrophage phagocytosis. Furthermore, new lesions seen on ultrasound may not also represent satellite lesions, as seen from the 1 patient who had pCR despite having a residual focal mass and new adjacent nodules worrisome for satellite tumor deposits on post-treatment ultrasound. Inability to distinguish viable tumor from post-treatment fibrosis or necrosis has contributed to the low sensitivity and poor positive predictive value of ultrasound in predicting pCR.

Changes in tumor enhancement following treatment may be a more accurate indication of treatment response and is likely the reason for breast MRI being superior to ultrasound for post-neoadjuvant chemotherapy tumor evaluation [14]. Resolution of contrast enhancement is indicative of reduced neo-angiogenic micro vessel density and permeability, implying reduced tumor activity, and changes in signal intensity and MR kinetics have been found to predict pathological response after initial cycles of chemotherapy [15,16]. Reduction in contrast enhancement was observed in all tumors in our study, demonstrating the effect of systemic treatment. The association between resolution of enhancement and pCR was not found statistically significant, possibly because of the small sample size, but it appeared to be relevant. We observed that none of the tumors that continued to show a significant degree of enhancement (although to a lesser extent compared to pre-treatment CT) had pCR. On the other hand, half tumors that no longer enhanced post-treatment were found to have pCR at surgery, whereas only 3 of 21 tumors with only minimal residual enhancement had pCR. While the absence of enhancement was not indicative of pCR, the presence of enhancement, however minimal, appeared significant even though inflammation and fibrosis within the treated tumor bed have also been known to enhance [17]. Residual tumors with complete resolution of enhancement cannot be assumed to be necrotic tumors, since residual invasive carcinoma, measuring 55mm in 1 case, was found in 11 instances in our study. However, this gross under-estimation of residual disease extent could be due to the large numbers of locally advanced tumors included in our study. One study reported that MRI tended to underestimate tumor size in tumors larger than T3, which made up 73% of the tumors in our study [10].

The sensitivity and specificity of CT in detecting residual disease was lower than that reported for MRI [10,14]. Similar to MRI, CT was more useful in detecting residual disease and 89% of our patients with focal lesions seen on CT were confirmed with residual disease. However, CT could not reliably predict for pCR and had a low positive predictive value (33.3%) and poor sensitivity (40.9%) in predicting pCR. Two-thirds of the patients with rCR on CT had residual disease, showing that CT was not useful in selecting complete responders. Given the small sample size, we were unable to further determine whether tumor subtype or the systemic treatment regimen influenced rCR rates or the prediction of pCR. We were also not able to determine whether post-treatment mammogram and ultrasound assessments would increase the accuracy of CT given the small numbers of women who also had post-treatment breast imaging. However, from our study, it would also appear that these modalities are better at detecting residual disease rather than pCR. CT appeared to be better at predicting the response in the nodes, with a much higher positive predictive value of 70.1%. However, even in those where complete nodal regression was reported on CT, 16 were found with residual nodal disease, with a median of 4 nodes involved. Many of these nodal deposits were less than 1cm in size, possibly explaining why they were not detected on CT. Among these 16 patients were 2 patients who were also reported with complete nodal regression on ultrasound, suggesting that even combined CT and ultrasound assessments were not sufficient to exclude residual nodal disease.

7. Conclusion

We observed a significant correlation between complete radiological response (rCR) on CT and complete pathological response (pCR), however two-thirds of those with rCR were still found with residual disease at surgery. Computed tomography scans had poor sensitivity and low positive predictive value in predicting for pCR. Residual enhancement was a significant factor, often being present when there was residual disease, but complete resolution of

enhancement in a residual mass correlated with pCR in only half the cases. This would support studies to evaluate the role of emerging modalities like contrast enhanced mammography, which adds functional capability to conventional mammogram.

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